The New England
Journal of Medicine

Copyright, 1943, by the Massachusetts Medical Society

VOLUME 228 APRIL 1, 1943 NUMBER 13

COMPOUND FRACTURES OF THE SKULL*

A Study of 104 Consecutive Patients

WILFRED PICKLES, M.D.†

PROVIDENCE, RHODE ISLAND

Je le pansay, Dieu le guarit.
[I dressed the wound, God healed it.]

REPEATED again and again in his writings, and making a memorial more lasting than the monument on which it is written, this phrase sums up Ambroise Paré's surgical beliefs.[1] Courage, humility and common sense changed this rustic barber's apprentice into the greatest surgeon of the sixteenth century. Long experience in wars as brutal and careless of human life as that now in progress taught him the value of letting well enough alone, and gave him his faith in the healing power of Nature. In his *Journeys in Diverse Places*, he[2] gives the following account:

> All the seigneurs within the town asked me to give special care, above all the rest, to M. de Pienne, who had been wounded, while on the breach, by a stone shot from a cannon, on the temple, with fracture and depression of the bone. They told me that so soon as he received the blow, he fell to the ground as dead, and cast forth blood by the mouth, nose and ears, with great vomiting, and was fourteen days without being able to speak or reason; also he had tremors of a spasmodic nature, and all his face was swelled and livid. He was trepanned at the side of the temporal muscle, over the frontal bone. I dressed him, with other surgeons, and God healed him; and to-day he is still living, thank God.

The passing of almost four hundred years has not changed the basic truth of the lessons learned and taught by Paré. New ways of "dressing the wound" have been found, but in no field of surgery is it more important to realize the need for avoiding irritation and for withholding meddlesome procedures than in the care of patients suffering from compound fractures of the skull.

The observations to follow are based on a study of 104 patients admitted to the Rhode Island Hospital between January, 1940, and July, 1942. The series includes, without further selection, all patients on whom a reasonable diagnosis of compound fracture of the skull was made. Ninety-eight of the diagnoses were made clinically; 6 were made by x-ray alone. Of the clinical diagnoses, 62 were confirmed by x-ray examination. It should be realized that an x-ray finding of fracture is not essential in making the diagnosis. The roentgen-ray examination is a most valuable aid, and should be used whenever possible, but one should take care not to be misled by lack of evidence of this sort. Many of the more seriously injured patients in this series were never in condition to warrant the use of x-rays; in several, fractures were found at operation that did not appear in the films, and definite clinical findings of compound fracture were not infrequently unconfirmed by careful x-ray examination. Insistence on x-ray evidence before accepting a diagnosis of compound fracture of the skull may result in real harm to the patient through improper treatment.

Although these patients have been selected for study on the basis of their having a special type of damage to the skull, one should not lose sight of the fact that they had an injury to the head, and that here, as in all patients with head injury, the degree and extent of the brain damage were of the greatest importance in treatment and prognosis. A compound fracture should be regarded as a major complication in a patient suffering from damage to the brain. By the classification adopted in a paper[3] read two years ago, 2 per cent of these 104 patients had concussion, 24 per cent had congestion, and 74 per cent had evidence of contusion, while 2 patients had no signs of brain damage. Comparing these figures with those for head injuries as a whole, 4 per cent of which had concussion, 47 per cent congestion, and 49 per cent contusion, the degree of brain damage, in general, is seen to be considerably severer in this group than in patients without this complication.

*Prepared for presentation at the canceled 1942 annual meeting of the New England Surgical Society.

†Surgeon, Neurosurgical Division, Rhode Island Hospital.

The small number of patients included in this study makes generalizations concerning age incidence of doubtful value. It may be of interest to note, however, that the ages ranged from one to eighty-three years, the most dangerous decades being from one to ten and from thirty-one to forty years. Forty-two per cent of the patients were injured in traffic accidents, 36 per cent in falls, and 19 per cent were struck in the head; 2 patients were hurt in airplane accidents, and 1 was wounded by a gunshot. Only 16 patients were injured in industrial accidents, in spite of the fact that the Rhode Island Hospital is located in a busy manufacturing center. Ninety per cent of all the injuries occurred in males.

A fracture is ordinarily held to be compound when, along with the break in the bone, there is a break in the overlying skin or mucous membrane such that infectious organisms are given a means of access to the fracture. When this commonly accepted definition is applied to fractures of the skull, compound fractures in this region fall naturally into three main groups — those of the base, of the paranasal sinuses and of the vault. Any classification of these fractures, unless so elaborate that it proves cumbersome, involves some overlapping and inaccuracy: several of the bones making up the base also help to form the vault, and lines of fracture may extend from one part to the other; fractures involving the sinuses not infrequently extend into the base; and multiple injuries add new difficulties. But this method divides these fractures into three definite clinical types, and is at least simple and workable.

Compound fractures of the base may affect the frontal, ethmoid, sphenoid, temporal or occipital bones; we have seen injuries in all these areas, but by far the greatest number are found to involve the petromastoid part of the temporal bone. Sixty-six of our patients had basal fractures, and 49 of these had damage in the petromastoid region. The diagnosis of compound basal fracture was made on the evidence of bleeding from the ear not otherwise explained, blood in the middle ear behind an intact drum, drainage of cerebrospinal fluid from the ear, bleeding into the pharynx not otherwise explained, x-ray films, or any combination of these. Bleeding from the nose was considered an unreliable indication, since the nasal bones are often broken without any fracture of the true skull. Nasal bleeding, however, should make one suspicious of skull damage. Patients with drainage of cerebrospinal fluid from the nose may have basal fracture or fracture involving the air sinuses; for the purposes of this study, they have been placed in the sinus group. X-ray confirmation of the diagnosis was obtained in 34 patients.

Basal skull fractures have, in general, a high mortality and a low probability of the patient's resuming a normal and useful life. When compounding, with the attendant risk of infection, is added, the outlook is considered even graver. But the condition of patients with compound basal fractures is by no means hopeless, and they well repay careful treatment. The treatment is primarily that of the associated brain damage. Many of these patients are in shock on admission, whereas others develop delayed shock. The blood pressure often holds up surprisingly well in patients whose vital functions are evidently depressed, only to fall suddenly when severe shock develops. We have come to consider the temperature as the most reliable indication of impending shock; any patient whose temperature is below normal is thought to be probably on the verge of shock. When shock exists or threatens, it must be treated before anything else. The patient is put to bed as quickly as possible; heaters and blankets are used to combat the fall in temperature; unless its presence interferes with necessary procedures the clothing is not removed, and then only under blankets without exposure; black coffee is given by rectum and caffeine with sodium benzoate under the skin. All unnecessary handling is avoided. X-ray examination is not attempted, and physical examination is strictly limited and is done without exposure. If there are fractures of the extremities they are fixed as simply as possible, with no attempt at correction. It is sometimes hard to convince the hospital staff of the importance of these measures, but their observance may mean the difference between life and death. Fluids are best replaced by the use of plasma; we are fortunate in having access to a supply of this substance. There is some evidence that the crystalline solutions used by vein in shock may increase the already heightened permeability of the smaller vessels and thus do harm.[4] If plasma is not available, therefore, or if hemorrhage is a real factor, it is wise to use transfusions of whole blood.

When the shock has been remedied the brain and skull damage can be treated. If the breathing is poor or the oxygen exchange is hampered, oxygen is given, preferably by the use of a Burgess[5] box. If the patient is excited, we omit the use of caffeine and give luminal sodium in the muscle. We do not use morphine, as we believe that this depresses respiration and raises intracranial pressure. When there is drainage of blood or cerebrospinal fluid from the ear, we use dry wipes to the auricle only; no attempt at cleaning out the canal or even examination is allowed until late in the course of treatment. The pharynx is kept clear of blood and mucus, when necessary, by position and

suction. If there is bleeding from the nose, we follow the same hands-off policy as in the case of the ear, hoping by these measures to avoid introducing infection. Lumbar puncture is not done on these patients until at least ten days after all discharge has stopped, as we believe that an outward flow is to be encouraged and that a possible reversal of flow by lowering the intracranial pressure may increase the chance of meningitis. For the same reason, we do not use dehydration. On the contrary, it is our belief that these patients need at least 2500 cc. of fluid, 5 gm. of sodium chloride, a proper supply of vitamins and 1500 calories daily. These are given by mouth when possible. If the patient is unconscious or unable to take liquids by mouth, they are given by the vein or by nasal stomach tube. We are convinced that many patients in this condition have, in the past, died of starvation and lack of fluids, and that giving proper amounts of liquid and nourishment will often keep the patient alive and allow Nature to "heal the wound."

Patients with fractures in the petromastoid region should be watched closely for the onset of infection. When a patient with such a fracture developed fever, it was formerly our practice to drain the mastoid process by operation, even though x-ray films showed no breakdown of the cells. With the advent of the sulfonamides, this procedure has become largely unnecessary, but we still follow it when the fever does not respond to treatment with the drug. Of the 66 patients in this series treated by these methods, 25 died, a mortality of 38 per cent. Twenty-one of these deaths occurred in the first twenty-four hours, many of them within an hour or two, so that there was little chance for any form of care to take effect. In the 45 patients who lived more than a day, 4 deaths occurred later, a mortality of 9 per cent. Two of these deaths were due to associated brain damage, and came on the third and fourth days respectively; 1 resulted on the twelfth day from a complicating subdural hematoma that was not recognized during life; and 1 came on the tenth day in a patient with acute mastoiditis, perisinus abscess and meningitis following fracture of the left mastoid process.

Compound fractures involving the paranasal sinuses may affect any of the air sinuses. Although it is likely that some of our patients classified as having compound fractures of the base had fractures entering into the ethmoid and sphenoid sinuses, we have not been able to recognize them definitely, either clinically[6] or by x-ray examination. From the standpoint of treatment, however, this is not of serious importance, since recognized fracture extending into either of these sinuses should be handled by the methods already outlined for fractures of the base. Twenty-one of the patients included in this study had fractures involving the air sinuses; in 10 patients, the maxillary antrum was affected, and in 11, the frontal sinus.

Wounds penetrating through the face into the antrum are, in our experience, rare; none were included in this series. When we have met such wounds, we have treated them by thorough débridement and cleansing, followed by a tight layer closure of the external wound, with drainage into the nose when needed. All the antral fractures in this study were of the closed type, and the diagnosis was made almost entirely on the basis of x-ray examination. The general treatment is that of the associated brain damage; locally, we have left these fractures alone, watching the patients carefully for the development of infection. In these 10 patients, there was no infection and no death resulted. There is always a considerable probability that fractures in this region may extend into the nearby basal areas; because of this, we withhold lumbar puncture for the same ten-day period that we observe in known fractures of the base.

Compound frontal-sinus injuries fall into three main groups: closed fractures, where the compounding is into the sinus itself, without an overlying scalp wound; open fractures, with an external wound extending down to the fracture; and penetrating injuries, where the scalp wound communicates directly with the cavity of the sinus. The closed fractures are treated in the same way as are basal and closed antral fractures. Open fractures are transformed into closed injuries by débridement, careful mechanical cleansing and layer suture without drainage, and are then treated as closed fractures. The most serious injuries in this region are those with penetration of the sinus cavity; these patients often have dural tears, contamination or gross damage of the frontal lobe, and injury of the orbit and its contents. It is our belief that here, as in other fields of surgery, the least extensive procedure that will serve the purpose is probably the best one to follow. As a result, we do not routinely remove the posterior wall of the sinus[7] or the entire lining mucous membrane,[8] nor do we drain any area from which damaged brain tissue has been removed.[7] Operation is done as early as possible. The external wound is débrided by the block excision of a hollow cone of damaged tissue about 0.6 cm. thick extending from the skin down to the bone, and any superficial loose bone fragments are removed. The instruments and gloves used in this dissection are then discarded, and the wound is flushed thoroughly with large amounts of sterile physiologic saline solution. In-driven

bone fragments or pieces that have evidently lost their blood supply are then removed; the one exception to this rule is in the case of the supraorbital ridge, which we have replaced on several occasions. Damaged brain tissue is removed by careful suction and an attempt is made to close the dura. This is often impossible because of tissue loss; when this condition exists, we wall off the part of the wound communicating with the brain by careful suture and close it without drainage. We have not used any foreign substance for dural closure,[9] as we have feared that any such material might encourage the development of infection. When the damage to the mucous membrane is not too great, we close it, after making sure that there is good drainage through the nasofrontal duct. If the mucous membrane cannot be closed, we remove the injured edges and make a layer closure of the wound over it around a small rubber-tissue drain. It has been said that external drainage must be avoided at all costs, as it will inevitably result in the formation of a fistula.[10] We have followed this method in 5 patients, removing the drain in a few days, when the danger of infection seemed to have passed; in each patient the wound healed well without further drainage. Eleven patients had compound fractures involving the frontal sinus; there were no deaths, and infection occurred in only 1 patient.

Drainage of spinal fluid through the nose is not infrequent in head injuries and may prove to be a serious complication; it always indicates a compound fracture, either of the base or of the air sinuses, and requires careful treatment. We have found conservative treatment to give good results. This consists of care of the general condition as already described and avoidance of any manipulation within the nose. Here again, we believe that the maintenance of an outward flow of fluid is important in avoiding infection; we do not use dehydration, and we delay lumbar puncture until ten days after all discharge has stopped. Five of our patients had definite leakage of cerebrospinal fluid from the nose; 1 died from severe brain damage within two hours; in all the others the drainage stopped in three to twelve days without the onset of infection. If a chronic draining fistula develops, it may be necessary to close the dural tear by one of the recognized methods. Up to the present time, we have not had occasion to do this.

Compound fractures of the vault divide themselves into three main groups: those without depression of the fractured bone; those with depression of the broken bone but without damage to the underlying dura; and those with injury of the dura and brain. In all of them, our basic aim is to change them into simple fractures of the skull, and then to treat the brain damage.

If the patient has a compound fracture without depression, we débride the wound by the method already discussed under fractures of the frontal sinus. If dirt has been ground into the surface of the skull, we try to remove it by thorough washing with saline solution or by swabbing with gauze; when this is not enough we use a curet or burr until we reach clean bone. Linear fractures are left alone unless hair or other foreign matter has been caught between the edges; in such patients, the contaminated edges are removed. The wound is then closed without drainage by a carefully made layer suture.

When there is depression of the skull without damage to the dura, the depression should be raised. In children it is often possible to make a burr hole alongside the depression, introduce an elevator through this hole, and snap the depressed fragments back into position. In adults this can rarely be done; it is usually necessary to remove the fragments piecemeal. In any event, free bone fragments or pieces that have lost their blood supply are taken out so that they may not act as foreign bodies. Any resulting bone defect can be repaired later if this proves to be needed. The uninjured dura is left alone unless there is evidence of blood under it, or unless there are neurologic signs making exploration advisable.

When, in addition to bone damage, there is injury to the dura and brain, we follow the methods developed by Cushing[11] as a result of his experience in World War I. The basic principle is the early removal of all foreign matter and all devitalized tissue. The wound is carefully débrided, saline washing is used freely, loose bone fragments are removed, and the damaged dural edges are trimmed off. Brain tissue that has been injured beyond recovery is removed by suction. If pieces of bone have been driven into the substance of the brain, they are sought for with a small rubber catheter; gentle irrigation and suction through the catheter will often dislodge them, and if this is not successful they can be removed with fine forceps. Exploration with the finger for such fragments is unwise. Damaged brain tissue along the track made by the bone is removed through the catheter in the same way. Our experience with penetrating wounds made by bullets or other missiles has been limited, as our patients were not suffering from war injuries; such wounds are treated, in general, in the same way as those caused by bone fragments. Horrax[12] has recently suggested an interesting modification of Cushing's method—the excision of the wound track by electrocoagula-

tion and strong suction. To date we have not had an opportunity to use this method. After the foreign bodies and damaged brain tissue have been removed, the dura is closed as well as possible, and the external wound is closed by careful suture in layers without drainage.

Seventeen patients had compound fractures of the vault. There were 4 deaths in this group, all from associated brain damage. No patient became infected.

The likelihood of infection in compound fractures is the chief difference between them and simple fractures. On the basis of our experience up to the present time, we believe that infection in compound fractures of the skull can be largely avoided by the following methods:

Minimal handling of the wound

When there is an external wound, we explore it gently with a sterile gloved finger to determine the presence of fracture. We then cover it with dry sterile gauze and do not try to clean it or its surroundings until we operate. When the wound involves the ear, nose or pharynx, we do not investigate or clean these cavities; we simply try to see that drainage from them is not blocked by any dressing.

Avoidance of reversal of drainage

We do not use lumbar puncture or dehydration until ten days after all bleeding or drainage of cerebrospinal fluid has stopped. In patients with compounding as shown by x-ray study but without external bleeding or drainage, we observe the same precautions until ten days after the injury.

Early operation

Our aim is to operate on patients needing such treatment within six hours of the time of injury. By using the methods already described the shocked patient can usually be made operable within this period. When the patient's condition is doubtful, we use transfusions of plasma or whole blood throughout the operation, with good results.

Thorough débridement and mechanical cleansing

We try to remove all foreign bodies and all contaminated or devitalized tissue by excision, curetting, washing with sterile saline solution and suction.

Avoidance of surgical drainage

All wounds, except those of the frontal sinus, are closed by careful suture in layers without drainage.

The advent of the sulfonamides has not lessened the basic importance of these methods. In injuries of this character, drugs will not take the place of careful surgery. They are useful in checking beginning infections or in treating established ones, but it is our belief that they should be used in the blood stream and given either by mouth or intravenously. There is evidence that they may be definitely irritating when they are used directly in the open wound.[13] If, for any reason, operation is delayed for over six hours, we sometimes dust the wound lightly with sulfanilamide powder, hoping thus to delay bacterial activity. At the time of operation, however, the chemical is removed along with other foreign bodies, and none of it is knowingly left in the wound.

In this series there was no wound infection. Two patients developed meningitis.[14] One of them, already mentioned, had a basal fracture through the mastoid process followed by acute mastoiditis, perisinus abscess and death from meningitis due to an unidentified organism. The other had an open fracture of the frontal sinus followed by pneumococcal meningitis, which cleared up with the use of sulfadiazine and antipneumococcus serum, the patient making a good recovery.

Operative treatment was used in 28 patients. Ten patients had débridement and suture and all recovered; 13 had débridement, elevation or removal of depressed or in-driven bone fragments and suture, and all of these recovered; 2 patients had complicating extradural bleeding and 1 of them died; 1 had a complicating subdural hematoma and died; 2 had exploration of the mastoid process, and both died. The operative incidence was thus 27 per cent, and the operative mortality was 14 per cent.

Summary

A study of 104 consecutive patients with compound fracture of the skull is presented.

As the main injury, 66 had fractures of the base, 21 had involvement of the paranasal sinuses, and 17 had injuries of the vault.

There was no wound infection, and 2 patients developed meningitis.

The operative incidence was 27 per cent, and the operative mortality 14 per cent. The overall mortality for the entire series was 28 per cent.

These patients were treated by methods aimed at guarding and helping the natural healing processes of the body.

Je le pansay, Dieu le guarit.

184 Waterman Street

References

1. Paré, A. Cited by Garrison, F. H. *An Introduction to the History of Medicine.* 996 pp. Philadelphia: W. B. Saunders Company. 1929. P. 224.

2. *Idem.* Cited by Paget, S. *Ambroise Paré and His Times, 1510–1590.* 309 pp. London: G. P. Putnam Sons. 1897. P. 59.
3. Pickles, W. Head injuries: observations based on a study of five hundred and fifty-four patients. *New Eng. J. Med.* **224**:139-142, 1941.
4. Andrus, W. De W. Present concepts of origin and treatment of traumatic shock. *Internat. Abstr. Surg.* **75**:161-175, 1942.
5. Burgess, A. M., and Burgess, A. M., Jr. New method of administering oxygen. *New Eng. J. Med.* **207**:1078-1082, 1932.
6. Rowbotham, G. F. *Acute Injuries of the Head.* 288 pp. Baltimore: Williams & Wilkins Company, 1942. P. 176.
7. Munro, D. *Cranio-cerebral Injuries: Their diagnosis and treatment.* 412 pp. New York: Oxford University Press, 1938. Pp. 160-164.
8. Gross, S. W., and Ehrlich, W. *Diagnosis and Treatment of Head Injuries.* 275 pp. New York: Paul B. Hoeber, Incorporated, 1940. Pp. 135-138.
9. Chao, Y. C., Humphreys, S., and Penfield, W. New method of preventing adhesions: use of amnioplastin after craniotomy. *Brit. M. J.* **1**:517-519, 1940.
10. Rowbotham.[6] Pp. 170-173.
11. Cushing, H. Penetrating wounds of the brain. *Brit. M. J.* **1**:221-226, 1918.
12. Horrax, G. Proposal for more radical treatment of gunshot wounds of the brain. *Canad. M. A. J.* **43**:320-324, 1940.
13. Pilcher, C., Angellucci, R., and Meacham, W. F. Convulsions produced by intracranial implantation of sulphathiazole: preliminary report. *J. A. M. A.* **119**:927, 1942.
14. Voris, H. C. Meningitis in head injuries. *Surg., Gynec. & Obst.* **75**:269-271, 1942.

A YARDSTICK FOR RHEUMATOID ARTHRITIS*

Applied to Patients Receiving Gold-Salt Therapy

THEODORE B. BAYLES, M.D.,† AND MARSHALL G. HELL, M.D.‡

BOSTON

"CHRONIC arthritis" is a term that has covered a multitude of joint conditions, and only fairly recently has a definite and intelligent division of the chronic arthritides been brought into being. However, to our mind the understanding of the various phases and of the as yet unpredictable course of rheumatoid arthritis leaves much to be desired, even in the minds of those most intimately associated with and well informed about the disease.

An analysis of fifty-four medical papers dealing with rheumatoid arthritis in seven leading medical journals for the years 1936 to 1940, inclusive, reveals that only one paper fails to separate in its discussion the two main arthritic groups of patients, that is, those with degenerative joint disease (hypertrophic arthritis or osteoarthritis) and rheumatoid (atrophic) arthritis. However, the division of rheumatoid arthritis into its active and inactive stages, admittedly difficult, was much less well handled. Forty-three of the fifty-four author-groups recognized the existence of these two stages of the disease, but only nine of the fifty-four attempted to analyze their case studies or therapeutic results, bearing in mind the difference between the active and inactive stages of the disease. This, it seems to us, is at once an understandable and yet deplorable condition. Certainly the study and treatment of chronic inactive rheumatic heart disease and the active rheumatic fever state are never considered simultaneously, yet the comparison of these two conditions with inactive and active rheumatoid arthritis does not seem farfetched. Realizing the inherent difficulties in such a division of these states, but believing that an attempt should be made to clarify the situation, we are presenting a simple objective numerical formula that is, in our experience, useful in separating the active and inactive stages of rheumatoid arthritis, and can be used as a therapeutic yardstick in the treatment of both the active and inactive stages of the disease. The application of this yardstick of therapy to the treatment of active rheumatoid arthritis with gold salts is presented here. The six more reliable commonly used objective clinical and laboratory observations in rheumatoid arthritis have been combined into what we have termed the "ADDICT chart" (Fig. 1). These are, in order of use, as follows:

A. *Functional Activity.* This has to do with the physical ability of the patient in its entirety. It is, in addition, a measure of whether the patient is or is not dependent on his family or the community. The subdivisions (0 through 4) are self-explanatory, and indicate physical as well as socioeconomic levels at which the patient exists at the time of the examination.

D. *Disease Activity.* This deals with the objective measurement of inflammatory changes that present themselves to the clinical observer at the time the patient is seen. The same range of subdivision as for functional activity has arbitrarily been set up, and the classic clinical signs of increasing joint inflammation used. For the measurement of changes subsequent to treatment or the status of the inflammation at any one time, it seemed wisest to use the patient's most active or inflamed joint as the one to be recorded. Varying degrees of activity are found in a number of different joints in the same patient, and joints that on pathological examination have appeared clinically inactive for years may show an active inflammatory process when examined microscopically. These facts make the use of D_1 of less practical value as an isolated observation, but if the simple criteria outlined in the chart are used and the relation of this measurement to the whole disease process is carefully reviewed, we believe that this figure is a useful approximation of disease activity.

D_2. *Deformity.* Deformity of a mechanical or static nature dependent on previous joint damage is recorded by the subdivisions. When subdivisions 1 and 2 are used,

*From the Medical Service of the Robert B. Brigham Hospital, Boston, and the Department of Medicine, Harvard Medical School.

†Research fellow, Robert B. Brigham Hospital; assistant in medicine, Harvard Medical School.

‡Visiting physician and director of research, Robert B. Brigham Hospital.

the examiner must be careful to ascertain that the periarticular thickening, painless swelling and crepitus or limitation of motion, or both, are due to static deformity, not to inflammatory changes about the joint. It is obvious that this objective observation in our formula is almost entirely a measure of mechanical deformity. The orthopedic treatment of inactive rheumatoid arthritic joint disease by surgery or with apparatus produces the largest change in this objective division of the chart. The worst joint is used in measuring improvement in this division. Since involvement of the upper or lower extremity may affect A (Functional Activity) to an unusual extent, it may be necessary in certain cases under "Remarks" to enlarge on the location of the worst joint and its importance to the patient; for example, ankylosis of the finger joint and that of a hip joint are quite different situations. However, in dealing with rheumatoid arthritis this is not so serious a difficulty as one might expect, because usually two or more joints of all those involved are at about the same stage of mechanical deformity.

FIGURE 1. *Chart for Coding Status of Arthritic Patients.*

CLASSIFICATION OF RATING	REMARKS
A — Activity of physical nature 0 = Employable 1 = Ambulatory (able to get about alone) 2 = Confined to one floor, bed and chair without assistance 3 = Confined to bed, needing part-time assistance (able to feed self, and so forth) 4 = Confined to bed, needing full-time assistance (helpless)	For hospitalized patients this rating is made on probable functional ability if the patient was discharged on the day of examination. For example if the patient is confined to bed because of an operation, the rating is either "3" or "4" depending on how sick the patient is.
D_1 — Disease activity 0 = None 1 = Tenderness or pain on motion or both 2 = Pain, tenderness and swelling 3 = Pain, tenderness, swelling and warmth 4 = A joint showing the maximum of acute symptoms (heat and redness added to the other signs)	*The rating should be made on the worst joint.* Care must be taken in deciding whether signs are due to disease activity or to the results of the disease. "Tenderness" is elicited by pressure of the fingers without squeezing or moving the bones. "Swelling" must be distinguished from fibrous thickening or painless effusion. "Warmth" must be natural and not due to treatment.
D_2 — Deformity of static nature 0 = None 1 = Periarticular thickening, painless fluid or crepitus on motion 2 = Limitation of motion 3 = Subluxation 4 = Ankylosis or flail joint	*The rating should be made on the worst joint.* Care must be taken to distinguish between real deformity and that due to disease activity, such as pain, which may in itself cause limitation of motion. If the disease is considered active these ratings can be made from a history of pre-existing, painless periarticular thickening or limitation of motion. "3" and "4" can be determined even if the disease is active and should be recorded if they exist.
I — Index of erythrocyte sedimentation 0 = 0.5 or less 1 = 0.6–1.0 2 = 1.1–1.5 3 = 1.6–2.0 4 = 2.1 or more	
C — Color of hemoglobin *Males* / *Females* 0 = 90–100 / 80–90 1 = 80–89 / 70–79 2 = 70–79 / 60–69 3 = 60–69 / 50–59 4 = 59 or less / 49 or less	
T — Tissue turgor (body weight) 0 = Normal or increased 1 = Loss 9 lb. or less 2 = Loss from 10 to 19 lb. 3 = Loss from 20 to 29 lb. 4 = Loss 30 lb. or more	The normal weight should be that which was average for the patient before the disease began, not the normal for age and height.

I. *Sedimentation Index.* This index, as well as other methods that measure the speed of erythrocytic sedimentation under standardized conditions, has long been recognized and proved to be a rough proportional measure of inflammatory activity in rheumatoid arthritis. We recognize that this is a rough laboratory measurement of a nonspecific physical state of the erythrocytes in the blood milieu. It errs grossly in certain individual cases, but on the whole is useful. Our subdivisions are arbitrary, but in our experience proportional to the activity of the disease. Change of the rate of erythrocytic sedimentation to a higher or lower level has been more useful than its absolute measurement in rheumatoid arthritis, a condition in which it is always eventually elevated.

C. *Hemoglobin Color.* The hemoglobin color or content of the blood is a moderately reliable laboratory measurement of rheumatoid arthritic activity in a large majority of patients. The presence of a hypochromic anemia that does not respond to iron therapy is frequent among patients with active rheumatoid arthritis, and its improve-

ment is of common occurrence in patients who become spontaneously better or respond to gold-salt therapy, as will be seen later on. The absence of anemia or a response of the abnormal condition to iron therapy usually indicates low-grade or early rheumatoid arthritic activity. The sex difference in normal values is used in making the subdivisions.

T. *Weight (Tissue)*. Body-weight or tissue change is the last objective observation in the formula, and as is true of all three of the absolute measurements, a change in the degree of abnormality is of more value than the single measurement. For the purpose of recording, the normal weight is the average weight during the years in the patient's life that she or he had good health. In children, the average weight for chronological age and height is used. As will be shown, a real change for the better in the first five measurements of this formula is practically always accompanied by a change in the same direction in this measurement. Rheumatoid arthritis in its active stage has been found to be associated with weight loss of some extent.

Illustrative Cases

As the question concerning the routine use of gold-salt therapy in rheumatoid arthritis is still unsettled, we shall not discuss the regime in detail. We shall point out what seem to be pertinent generalizations as they apply to the selection of patients and their treatment and to the end results. The cases are used to illustrate our chart, not to defend or abuse gold-salt therapy in rheumatoid arthritis. The use of this treatment at the Robert B. Brigham Hospital has been, and still is, considered a research problem that is in progress.*

Case 1 (R. B. B. H. 1847) is that of a twenty-one-year-old stenographer with rheumatoid arthritis of twenty-one months' duration who was admitted for gold-salt therapy after a previous admission and follow-up study in the clinic. During the twenty-one months before the second admission, the patient had become progressively worse until she was barely able to get in a chair for part of the day.

Figure 2. *Chart of Case 1.*

Date	A	D_1	D_2	I	C	T	Location	Remarks
6/25/40	3	3	2	3	2	1	Hospital	Second admission; arthritis 21 mo.
7/10/40	3	3	2	3	2	1	Hospital	Before gold salts
9/23/40	1	1	2	1	1	0	Hospital	After gold salts
12/ 2/40	1	1	2	1	0	0	Home	3 mo. later
3/ 1/42	0	0	2	1	0	0	Working	18 mo. later

Figure 2 illustrates the course that this patient followed for the eighteen months after therapy. There was a satisfactory response, which has persisted. As a relatively early case, the objective measurements all improved except D_2, which measured the mechanical deformity of limitation of motion in the knees. Despite this deformity, which is permanent, owing to fibrous-tissue adhesions and some joint damage, the patient has been able to become self-supporting (A), has no signs of disease activity in her joints (D_1), has gained weight (T), has lost her anemia (C) and is essentially a well person objectively except for the borderline abnormal sedimentation index (I) and the aforesaid mechanical deformity.

Figures 3 and 4 (Cases 2—R. B. B. H. 1910—and 3—R. B. B. H. 1917) represent the use of our curve in 2 other patients with active rheumatoid arthritis who were badly crippled because of the inflammatory aspect of the disease, but with some degree of mechanical deformity. The patient in Case 3, a fifty-nine-year-old woman, became active following a course of gold salts. However, ten months later the chart figures show a definite return of arthritic activity, for which a second course of gold-salt therapy is being administered.

Figure 3. *Chart of Case 2.*

Date	A	D_1	D_2	I	C	T	Location	Remarks
11/ 7/39	2	3	2	2	1	3	Hospital	Admission; arthritis 48 mo.
4/11/40	2	2	2	2	1	2	Hospital	Before gold salts
6/29/40	0	0	2	1	0	1	Hospital	After gold salts
2/ 4/41	0	0	2	0	0	0	Working	8 mo. later
3/ 1/42	0	0	2	1	0	0	Working	21 mo. later

Figure 4. *Chart of Case 3.*

Date	A	D_1	D_2	I	C	T	Location	Remarks
3/23/40	4	3	2	3	2	4	Hospital	Admission; arthritis 6 mo
4/11/40	4	3	2	3	2	4	Hospital	Before gold salts
7/16/40	2	2	2	1	2	1	Hospital	After gold salts
12/19/40	0	0	2	0	0	0	Working	5 mo. later
2/27/41	0	1	2	1	0	0	Working	7 mo. later
5/10/41	4	3	2	3	2	2	Home	10 mo. later

It should be noted that in neither of these cases did mechanical deformity (D_2) improve, and that the rather temporary response in Case 3 may have been a spontaneous remission rather than the response to the gold medicament. Certainly the response in the second course of treatment has not been so dramatic as in the first.

Figure 5 (Case 4—R. B. B. H. 1803) shows what happened during the course of the second admission of a thirty-eight-year-old Italian housewife who received the routine procedures of good diet with extra vitamins, rest, physiotherapy, orthopedic devices and so forth for four months, with the only change in her chart a shift in A from 4 to 3. With gold therapy there was an appreciable change for the better. Despite what was definite improvement, certain numbers in the

*In the presence of essentially normal blood and urinary findings and in the absence of a history of kidney or liver disease or a sensitivity to drugs, these patients with active rheumatoid arthritis received one 25-mg. dose, one 50-mg. dose and nineteen 100-mg. doses weekly of a soluble intramuscular preparation (gold content, 50 per cent). This gave a total of 1975 mg. over a period of twenty-one weeks. Complete blood examinations, sedimentation indices and urinalyses were done weekly. All the patients were hospitalized for this therapy.

chart that signify low-grade activity have persisted at a low level, and these have kept the patient's

FIGURE 5. *Chart of Case 4.*

DATE	A	D_1	D_2	I	C	T	LOCATION	REMARKS
1/18/40	4	3	2	2	1	2	Hospital	Second admission; arthritis 17 mo.
5/ 5/40	3	3	2	2	1	2	Hospital	Before gold salts
7/30/40	1	1	2	1	1	1	Hospital	After gold salts
10/24/40	1	1	2	1	1	1	Home	3 mo. later
3/ 1/42	1	1	2	1	1	0	Home	18 mo. later

functional activity from becoming normal, although she is taking care of her family.

Case 5 (R. B. B. H. 1978) was that of a fifteen-year-old schoolboy with active rheumatoid arthritis (Still's disease). He did not respond to gold-salt therapy, as shown by the chart (Fig. 6), but did

FIGURE 6. *Chart of Case 5.*

DATE	A	D_1	D_2	I	C	T	LOCATION	REMARKS
2/26/40	4	3	2	3	2	4	Hospital	Admission; arthritis 4 mo.
9/ 6/40	4	3	2	3	2	4	Hospital	Before gold salts
12/18/40	4	3	3	3	2	4	Hospital	After gold salts
4/ 1/41	3	2	3	2	1	3	Hospital	4 mo. later
7/ 1/41	3	2	2	2	0	2	Hospital	7 mo. later
3/ 1/42	2	1	2	2	0	0	Home	15 mo. later

undergo what was probably a normal remission some months after the end of therapy, and the chart then followed the same type of response as seen in patients who responded to gold salts. Here again, a large part of the mechanical deformity persisted, but subluxation (D_2) was corrected by vigorous orthopedic treatment. In this case, seven months of routine therapy had produced no change for the better, as shown by the chart, and this was obvious from a clinical study of the patient; nor did gold therapy produce any real improvement. However, when a spontaneous remission occurred the chart portrayed the fact that the patient was improved enough to be allowed home to plan some vocational training.

Case 6 (R. B. B. H. 1899) portrayed in Figure 7, was that of a forty-year-old man with marked mechanical deformity and a relatively low-grade arthritis. There was no change after eight months

FIGURE 7. *Chart of Case 6.*

DATE	A	D_1	D_2	I	C	T	LOCATION	REMARKS
10/24/39	3	2	3	2	1	2	Hospital	Admission; arthritis 36 mo.
6/25/40	3	2	3	2	1	2	Hospital	Before gold salts
9/23/40	3	2	3	1	0	0	Hospital	After gold salts
12/ 2/40	3	2	3	1	0	0	Hospital	3 mo. later
2/21/40	2	2	3	1	0	0	Hospital	5 mo. later

of routine therapy. The change after gold-salt therapy is illustrative of what occurs in patients with marked mechanical deformity who improve with gold salts or spontaneously, usually over a long period of time. The objective measurements of inflammation or arthritic activity (D_1, I, C and T) changed in this patient for the better, but the joint damage was sufficient to cripple permanently or at least to handicap him.

The last case illustrates a general rule that we have found useful in selecting patients for different kinds of therapy. The patients who require medical care, such as bed rest, better nutrition, mild physiotherapy, resting shells and so forth, are those in whom D_1, I, C and T are high; this group should be considered for gold-salt treatment. The patients in whom the mechanical deformity, not joint inflammation, is a main factor must be treated by vigorous physiotherapy, orthopedic appliances and surgery; gold-salt treatment will not help this group. These two phases of the disease are represented in Case 6. Gold-salt therapy, hand in hand with optimum general medical treatment, caused a relative disappearance of arthritic activity. Vigorous muscle exercises in bed and in the tank and the use of orthopedic appliances, such as iron calipers for the knees, then allowed the patient to improve his functional level (A) from "bed and chair" to "ambulatory — confined to one floor." This was possible despite the continued subluxation of the knees. Further orthopedic attack, such as arthroplasty of the knees, might improve the functional activity to a still better level.

Since the cases presented in this paper seem to have done well following gold-salt therapy, we emphasize again that in Cases 1 and 2 the satisfactory response could be attributed to this form of therapy. Case 3 may well have had a spontaneous remission. Cases 4 and 6 improved only slightly during gold-salt therapy, and in Case 5 there was no response to it. In addition, 3 of these patients showed minor toxic heavy-metal effects, such as small ulcerations in the mouth and a slight dermatitis when exposed to the sun. A subsequent series of patients receiving smaller and consequently less toxic amounts have not shown marked changes in their charts.

SUMMARY

A simple numerical chart for use in studying the course of rheumatoid arthritis is presented. As its objective measurements are an indication of the presence or absence of arthritic activity, it can aid in determining the most useful therapeutic approach for a particular patient.

The use of the chart as a therapeutic yardstick for the response or lack of response of rheumatoid arthritis to gold-salt therapy is illustrated by case reports.

MEDICAL PROGRESS

NEUROLOGY

JAMES B. AYER, M.D.*

BOSTON

SO MANY topics pertaining to neurology have appeared in earlier Progress Reports that it is difficult not to duplicate. With an attempt to avoid duplication or with approach from a different angle, a miscellaneous group of subjects for discussion has been chosen, which I have found of interest and which may not be too old a story for the reader.

REACTION OF NERVOUS SYSTEM TO SULFONAMIDES

Reactions following the use of three sulfonamide drugs were listed in 1941 in a circular letter of the National Research Council.[1] Besides the relatively common effects on the blood and kidneys, the following concerned the nervous system:

EFFECT	SULFANILAMIDE	SULFAPYRIDINE	SULFATHIAZOLE
Nausea and vomiting...	Fairly common	Frequent	Uncommon
Dizziness	Common	Common	Uncommon
Psychosis	0.6% of cases	0.3% of cases	Very rare
Neuritis	Very rare	Not reported	Rare
Ocular or auditory....	Rare	Rare	Rare

Since this report sulfadiazine has come into common use. In their report on the Halifax epidemic of meningococcal meningitis, in which a phenomenal therapeutic success was registered, Dingle et al.[2] state that nausea, vomiting, dermatitis, cyanosis or mental symptoms attributable to the drug were not present. Finland et al.[3] in a paper concerned largely with the toxic effects of sulfadiazine give their conclusions based on 446 cases. They find the toxic symptoms from this drug to be "relatively mild and infrequent," although nausea and vomiting did occur in 9 per cent of cases. There was no note on a deleterious effect on the central or peripheral nervous system. A second paper emanating from the same source,[4] and concerning a group of 460 patients treated with sulfadiazine, states that toxic reactions on the nervous system were limited to 2 patients. One of these was an alcoholic with pneumonia who showed delirium on the seventh day of treatment; the drug was stopped, and when given again three days later the delirium did not recur. The other patient was disoriented and confabulated on the third day of treatment after taking 18 gm., with a blood level of 16 mg. per 100 cc. On the stopping of medication the symptoms cleared. No patient developed peripheral neuritis.

In a recent exhaustive study on the sulfonamides, Janeway,[5] although listing the above nervous symptoms, implies that they have been reduced since the advent of sulfadiazine. However, he adds one more symptom to the list when he states: "An important practical point is that an ambulatory patient taking sulfonamides should be warned that his reaction time may be slowed. Special care should be observed in driving a car, crossing streets and performing manual work." This writer, with others, mentions two important points to be kept in mind concerning the development of toxic symptoms of any type: hypersensitiveness to the drug, either natural or following the previous use of a sulfonamide, and the late insidious development of toxic symptoms, sometimes even after the drug has been stopped. This second warning is especially directed to sulfadiazine because, as Janeway states, it produces severe reactions less frequently than sulfathiazole and is treacherous because of its slow excretion.

A case with a fatal outcome well known to me[6] illustrates the insidious advent of toxic reactions in a patient probably sensitized to sulfa-drugs. This patient, a healthy although mildly hypothyroid woman of fifty-nine, was given sulfathiazole for urinary infection and later, because of unexplained fever, sulfanilamide, which was later changed to sulfadiazine; a total of approximately 30 gm. of all three drugs was administered. She then rapidly lapsed into a lethargic state, which continued until death two weeks later. During this period somnolence was the cardinal symptom, from which the patient could be awakened for a few minutes only, when she would recognize attendants and relatives. Although somewhat disoriented she could hardly be considered otherwise psychotic, offered no complaints except excessive fatigue, and showed no neurologic signs. Post-mortem examination revealed characteristic sulfonamide nephrosis. The brain was grossly normal, but micro-

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*. Volume III. 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. $5.00).

*Professor of neurology, Harvard Medical School; chief of Neurological Service, Massachusetts General Hospital.

scopic examination showed diffuse toxic effects on both nerve cells and neuroglia.

Peripheral neuritis and spinal-cord lesions have been reported. Bieter et al.[7] cite 2 cases of the former from sulfanilamide, and also mentions experimental injections in chickens following which peripheral neuritis ensued, and a case reported by Tolosa and Savoy.[8] Ornsteen and Fürst[9] found a neuritis with a distribution like that of progressive muscular dystrophy following the ingestion of 130 gm. of sulfanilamide in the course of thirty-five days. Elkington[10] reports serious peripheral nerve damage following the intramuscular injection of sodium sulfapyridine, and naturally warns against its use in proximity to nerves. Cerebral symptoms simulating those of acute meningitis are described by Johnstone and Forgacs[11] from sulfapyridine, and a hemorrhagic encephalopathy was seen by Roseman and Aring[12] from the use of sulfamethylthiazole.

Several papers concern acute visual disturbance during the course of treatment by sulfonamide drugs. Blankstein[13] attributes his case to an acute myopia, due, he believes, either to allergy or to a difference in osmotic tension of the lens as compared with the aqueous humor produced by the unequal distribution of sulfanilamide within the eye.

Little[14] lists the following nervous and mental complications that have been reported: dysmorphopsia, aphasia, agraphia, stammering, toxic psychosis, peripheral neuritis, encephalomyelitis, myelitis, optic neuritis, transitory myopia, meningeal signs, blindness and convulsions. Such an array of serious by-effects is at first startling, but it should be remembered that these complications occurred with sulfonamide drugs now abandoned, and in dosages that are no longer acceptable. Against this implication that sulfonamide drugs are extremely toxic to the nervous system is the experience of Finland, already mentioned, with 906 patients treated with sulfadiazine in only 2 of whom nervous-system symptoms developed. Little himself, although listing these serious effects, makes some explanation when he says, "The drugs appear more neurotoxic in the presence of preexisting disease of the nervous system." He also states, as does Janeway, that the intermittent administration of a single sulfonamide or successive administration of different sulfonamides seems to predispose to the development of toxic nervous-system symptoms.

In conclusion, mild and severe toxic symptoms referable to the nervous system must be recognized as ever-present possibilities, especially if the patient has latent or declared disease of the brain or spinal cord. However, with care as to the choice of drug and dosage serious sequelae can usually be avoided.

Local Use of Sulfonamides within Cranium

The neurosurgeon would like to have a safe antiseptic to apply locally or over the dura, either as prophylaxis or in the presence of infection, and it is natural that he should wish to use a sulfonamide drug that theoretically should be effective against the bacteria ordinarily encountered.

If one is familiar with the history of numerous liquid antiseptics that have been injected into the subarachnoid space, both in animals and in man, in different types of meningitis and also in uninfected laboratory animals, he will approach the subject with great skepticism. The conclusions forced on the older investigators — for the subject has been generally banned for years — were that all antiseptics did harm and no good.[15] But the sulfonamide drugs are not antiseptics comparable to corrosive sublimate, lysol and so forth, and perhaps this prejudice is unfounded. I have myself used penicillin intracisternally in pneumococcal meningitis, without apparent harm.

Present interest concerns the toxicity, irritability and usefulness of sulfonamide powders placed directly on the brain cortex and over the dura, and there are at hand four reports using apparently similar technics, but with disagreement concerning results. Watt and Alexander[16] applied sulfathiazole powder epidurally in the case of 6 frontal craniotomies. In 5, epilepsy occurred promptly. In the remaining case, in which epilepsy did not appear, the dura at this point had not been opened. The conclusion seemed obvious that seepage of the drug through the dural opening was the cause of the epilepsy. Experiments on cats substantiated the results in man. Other sulfanilamide drugs so used did not produce epilepsy, nor did sulfathiazole used similarly but in posterior craniotomies cause epilepsy.

Pilcher et al.,[17] experimenting with cats and rabbits, placed sulfathiazole powder directly over the cortex and closed the dura over it. In 36 animals almost all had focal epileptic seizures, which became generalized. Fits were not produced by sulfadiazine or kaolin used as a control, and only once by sulfanilamide. At autopsy weeks or months later the drugs were found in hard plaques adherent to the cortex. At no time did the drugs appear in the blood or spinal fluid in appreciable amounts.

These two papers are in essential agreement that epilepsy results from the local use of sulfathiazole powder when placed on or near the cerebral cortex.

Hurteau[18, 19] placed various sulfonamide drugs in small, aseptically prepared wounds of the cortex and subsequently covered the wounds with dura. He does not mention epilepsy as resulting from

these experiments. On examination he found little reaction of the brain or meninges; well preserved nerve cells could be seen near the margin of the wounds, and there was minimal meningeal reaction. The rate of absorption was most rapid with sulfanilamide and slowest with sulfapyridine, with sulfathiazole and sulfadiazine intermediate.

Ingraham and Alexander[20] superficially traumatized the cortex in 7 cats and 3 monkeys, some with aseptic and some with nonsterile technic. Powders of sulfanilamide, sulfathiazole and sulfadiazine were applied to the traumatized cortices and the animals were killed in three to five weeks. Epilepsy was not observed. In general there was surprisingly little reaction to the drugs.

It is obvious that with such contradictory results much more work will have to be done before the local use of sulfonamide drugs can be considered either safe or advantageous.

Myasthenia Gravis

Operative removal of the thymus gland as a cure for myasthenia gravis has recently received considerable notice, especially since the publication of the paper of Blalock et al.[21] in 1941. It has been suspected for many years that there may be a relation between the thymus gland and myasthenia, because of the finding of an enlarged gland or a thymic tumor in this disease at autopsy. Poer[22] states that in a total of 129 autopsies and operations in myasthenic cases enlargement of the thymus gland was found in 71 cases, an incidence of 55 per cent. In 1939 Blalock et al.[23] reported a case that was said to be the "fifth instance of an attempt to influence the course of myasthenia by an operation on the thymus." This was a removal of a cystic tumor. The patient was reported as entirely well four years later. Since then Campbell[24] has removed two thymomas, one a large cystic tumor, the patient doing well two years after operation but still taking Prostigmine. Turnbull[25] removed a malignant thymoma without benefit, and Poer[22] a malignant thymic tumor with improvement over a period of four months.

Encouraged by success in the removal of a cystic tumor, Blalock et al.[21] turned to another aspect of the subject. Removal of thymic tissue in which no tumor could be discovered was carried out in 6 cases. In 5 of these, definite hyperplasia was present, but no tumor. The early results were gratifying, but an addendum to this paper states that only 3 of the 6 patients continued to show improvement from the operation.

Four patients chosen with care because of constancy of symptoms have been subjected to thymectomy at the Massachusetts General Hospital. No tumors were expected and none were found. The results have so far not been encouraging.[26]

In appraising the value of operations on the thymus gland for myasthenia gravis, one must clearly distinguish between three conditions: malignant tumors of the gland, hypertrophy, and degenerative states and remnants. As pathological classification is as yet not too clearly defined, and physiologic tests for the function of thymic tissue are not yet available, the effect of thymus-gland excision cannot at present be properly evaluated. Thus far the most striking improvement in the course of myasthenia has been reported from excision of cystic and malignant thymus glands, the excision of the normal or hypertrophied gland still awaits evaluation, and that of thymic remnants seems to offer the least benefit. Further operations must precede a proper conception of the thymus gland in relation to myasthenia gravis.

X-ray therapy of enlarged thymus glands was at one time recommended. In 1923 Mella[27] published the report of such a case. A woman of twenty-three presented herself with progressive difficulty in swallowing, chewing and speaking. A typical myasthenic reaction to faradism was obtained. X-ray disclosed a precardiac shadow that was considered consistent with an enlarged thymus gland. Thirteen months after the onset of symptoms, at this time incapacitating, x-ray treatment was inaugurated, the patient receiving four suberythema doses at three-week intervals, directed to the thymus gland. In five weeks she was much better; in one year she was well and working, and electrical reactions were normal. This patient returned to the hospital four months ago, twenty years after her first admission, because of another complaint; she was free from all myasthenic symptoms. Further evidence that the diagnosis was probably correct was given by her; four years previously immediately following a pelvic operation under spinal anesthesia she had experienced a transitory drooping of the eyelids and difficulty in swallowing and talking. In this case there was only x-ray evidence of a shadow in the region of the thymus gland, which was said to have disappeared after x-ray therapy. The symptoms were highly suggestive of myasthenia gravis, and after persisting for more than a year disappeared following x-ray treatment. It seems reasonable to entertain a probable relation between the thymus gland and myasthenic symptoms.

Pregnancy has been thought to affect the course of myasthenia gravis. Sometimes it is said to produce relapse and sometimes remission. Viets et al.[28] in their large and well-controlled series present 8 cases in which remission during pregnancy was the rule, making possible a reduction in medica-

tion or even discontinuance of the drug. Improvement usually began soon after conception and lasted until well along in the puerperium. Rarely an increase of myasthenic symptoms occurred; if so, it was early in the course of pregnancy and was not severe. These authors believe that pregnancy, labor and nursing do not affect the course of the disease unfavorably, and they do not advocate early abortion, as has been advised and practiced by some.

In this connection there is an extremely interesting report of a myasthenic baby born of a myasthenic mother.[29] As in Viets's cases, the mother, whose condition conformed in every way to the diagnosis of myasthenia gravis, went through pregnancy without incident, although it was necessary to increase the dose of Prostigmine slightly. The baby weighed seven pounds, eight ounces, at birth and appeared well formed and normal until the third day, when difficulty was experienced in taking its formula. On the fourth day its face was masklike, the jaw drooped, the cry was almost noiseless, and mucus collected in the throat. The response to 4 mg. of Prostigmine in milk was dramatic; all symptoms disappeared and the baby nursed normally. In spite of persistent use of Prostigmine sudden death occurred on the seventh day after birth. So far as known, this is the first case suggesting the hereditary transmission of myasthenia gravis.

The age of onset of symptoms of myasthenia gravis has been set much earlier than previous statistics indicated. Although commonly recognized as a disease of youth and young adults, ten years is usually considered the low limit of age. The case just quoted, showing myasthenic symptoms at birth, and another case[30] with onset at five years change the conception of the age incidence. That myasthenia gravis is not only hereditary but also familial is suggested by Riley and Frocht,[31] who report two sisters with onset at eleven and fourteen years respectively. The disease has usually been considered neither hereditary nor familial.

Although the importance of the Prostigmine test in the diagnosis of myasthenia gravis is now a matter of common knowledge, it may well be called to mind again for there are numerous other conditions manifesting muscular weakness that are easily confused with it. As time goes on, the prompt improvement seen on administering this drug in myasthenia gravis is so dramatic that Prostigmine may well be considered specific. In no other disorder does one see more than slight benefit, and in some conditions, notably bulbar paralysis, exaggeration of the paralysis may occur. It is well therefore to emphasize the Prostigmine test elaborated by Schwab and Viets[32] as a diagnostic test for myasthenia gravis. The test consists of a point-scale estimate of objective and subjective improvement in the various symptoms before and after the intramuscular injection of 1.5 mg. (1/40 gr.) of Prostigmine Methylsulfate and 0.6 mg. (1/100 gr.) of atropine — ampules containing these amounts and marked for diagnostic use are obtainable. Examinations are made every ten minutes for an hour, and improvement is recorded on a scale ranging from "1" to "5." As stated above, this test may be dangerous in bulbar palsy, because of increased difficulty in breathing. and choking. It should therefore not be used at all in such cases, or the dose should be smaller than otherwise.

Metastatic Cancer

It requires an enthusiast to discuss metastatic cancer in any location, particularly when the tumors lie within the cranial cavity or the spine. Patients so afflicted are the despair of relatives and physicians alike, for the inability to bring to them any useful therapy — other than morphine — is the general rule. Even textbooks on neurology pay scant attention to these cases, and yet they offer a constant challenge in differential diagnosis. Experience shows that metastasis to the brain is often mistaken in its early stage for a vascular accident, encephalitis or some other disease. Even though a primary malignant growth is found elsewhere in the body, it is not sound reasoning to assume that coexisting cerebral symptoms must also be due to metastasis. It is, of course, recognized that the lung is the seat of primary or secondary malignancy that ultimately finds its way to the brain, yet how often one forgets to study the lung for this evidence, and how often one fails to find it when it is looked for. Although not certain in its diagnostic role, x-ray examination of the lung usually shows a shadow characteristic or at least suggestive of carcinoma, and it is now a rule, sometimes forgotten because of lack of pulmonary symptoms, to call in this evidence in suspected brain tumor.

Carcinoma of the lung and brain metastasis. One of the commonest types of brain metastasis is that derived from bronchogenic carcinoma. It is also a type frequently mistaken in its early period, for two chief reasons: because the early symptoms are not usually characteristic of tumor of the brain, and because pulmonary symptoms are either minimal or absent and x-ray signs are noncommittal. A review of this subject by King and Ford[33] is therefore welcome. Of 100 cases studied at the Johns Hopkins Hospital and coming to autopsy, 27 showed metastasis to the central nervous system. The age incidence was forty to sixty years; the sexes

were equally distributed. Metastasis to the brain occurred early, and in 14 cases cerebral symptoms dominated the clinical picture, antedating the pulmonary symptoms. The lesions found were usually multiple and small, the cortex, white matter, brain stem, hypothalamus, cerebellum and meninges being indiscriminately the seat of invasion. Less commonly a large solitary tumor (4 cm. or more in diameter) was found. Initial symptoms and signs were of two general types; more commonly they were mild and indefinite in character and location and were associated with mental disturbance, but not infrequently a rapid onset suggestive of embolus, thrombosis or hemorrhage, was noted, and occasionally the first symptom was a convulsion followed by hemiplegia. Although headache was usually present, papilledema was rare, occurring in only 5 of the 27 cases, and the spinal fluid generally failed to show elevation of pressure, although increase in fluid protein was the rule. X-ray films of the skull were negative except in the event of bone involvement.

Globus and Meltzer[34] have recently analyzed 57 cases in which autopsy revealed metastatic growth. Many of their statistics are worth while having in mind for the purpose of differential diagnosis. These authors found a percentage of metastatic lung cancer even higher than is generally supposed. Of 33 cases where complete autopsy was available, 19 were from this source. The fact that in 49 of the 57 cases the brain showed carcinomatous metastasis is no surprise, but that metastasis was single in 39 per cent of all cases is contrary to the general impression. On the clinical side, Globus and Meltzer emphasize the well-known fact that papilledema is usually absent or only of moderate degree and that spinal-fluid examination is seldom helpful.

For the clinician these two papers are extremely helpful, for the early manifestations of metastatic tumor of the brain are seldom clear cut. Especially must one be reminded to examine the lungs with great care in patients suspected of having brain tumor.

Carcinoma of prostate and metastasis to spine. The feeling of helplessness in the presence of metastatic cancer has at last been tentatively relieved by the dramatic effect of orchidectomy on carcinoma of the prostate. Although the general subject has recently been treated in these reviews by Quinby,[35] it is perhaps not amiss to emphasize the beneficial effects of this procedure on the pain of nerve-root involvement, and to add a note on a case known to me.

The beneficial effects of orchidectomy and of diethylstilbestrol on carcinoma of the prostate have during the past year been the subject of more than one symposium of urologists. In particular the papers of Huggins and his associates,[36] Alyea and Henderson,[37] Chute, Willetts and Gens[38] and Nesbit and Cummings[39] and discussion by various surgeons may be cited as in general agreement that orchidectomy causes an involution of carcinoma of the prostate, and where metastasis to the spine is present prompt relief of pain occurs. For the most part there is general agreement that bony metastases in the spine and pelvis also regress, and x-ray evidence of the healing of such lesions is offered. There is a difference in opinion whether to employ diethylstilbestrol before or along with castration, and the relative merits of the operative as compared with the hormonal effect on the tumor are not yet settled.

None of the writers mentioned deal with the subject from a neurologic point of view; they do not state whether the metastasis was limited to the spine or to the intervertebral foramina, or was intraspinal. In a case known to me the metastasis was shown to be definitely within the spinal canal. Relief from pain and removal of the spinal-fluid block, first after diethylstilbestrol medication, and subsequently as a result of castration, gave objective evidence of the beneficial effect of both these therapeutic agents on an intraspinal tumor. The following abstract of this case, reported by Clarke and Viets,[40] is instructive:

> A 69-year-old man had noted pain in the legs and difficulty in walking for six months. Physical examination revealed tenderness over the lumbar spine, lumbar lordosis, absent knee and ankle jerks and an enlarged prostate, a needle biopsy of which showed carcinoma. X-ray films gave evidence of metastasis to the lumbar spine. Lumbar punctures at the lowest dorsal and lowest lumbar levels showed partial dynamic block, and the fluid from the lower puncture contained 798 mg. of protein per 100 cc. Four days after the beginning of diethylstilbestrol therapy the patient was free from pain and ambulatory, and 8 days later the spinal-fluid dynamics and protein and the neurologic findings had returned to normal. He returned to work, and 11 weeks after the beginning of therapy the prostate had diminished in size and another lumbar puncture showed no evidence of block and a normal spinal-fluid protein. The diethylstilbestrol was discontinued. The patient continued work for 4 months, when the pain and difficulty in gait returned and lumbar puncture revealed complete dynamic block and a protein of 7500 mg. per 100 cc. in the spinal fluid from the lower needle. Orchidectomy was performed, and 5 days later the symptoms were completely relieved. Twelve days later the spinal-fluid dynamics were normal and the protein was 80 mg. per 100 cc. When last seen, 6 weeks after operation, the patient was free of pain.

Sufficient time has not elapsed to estimate the late effects of this treatment. Even if a long-time cure is not forthcoming, the immediate effect is far

better than was possible by neurosurgery, x-ray therapy or medication. Furthermore, a line of hopeful research has been opened into the pathogenesis of other forms of malignant disease.

Thyrotoxic Myopathy

Thyrotoxic myopathy, an unusual condition, but one in which the unfortunate diagnosis of progressive muscular atrophy is apt to be made, is discussed by McEachern and Ross.[41] Although rare, this syndrome should be recognized early, as a cure may be expected from treatment, and unrecognized cases go on to death.

These authors analyze 13 cases — 10 from the literature and 3 of their own. The similarity of the clinical picture in all cases is striking, and may be described succinctly as that of toxic goiter in addition to an exaggerated state of progressive muscular atrophy. The patients are usually middle-aged men who present themselves complaining of excessive fatigue and loss of weight during a period of weeks or months. Most conspicuous is generalized muscular wasting associated with gross muscular twitching. The patient also perspires freely, runs a rapid pulse, and shows a fine tremor of the outstretched hands — this in addition to the muscle fasciculation. There may or may not be exophthalmos and enlargement of the thyroid gland. The basal metabolic rate is elevated, but not excessively so (+14 to +68 per cent in 12 cases, +100 per cent in 1 case). Favorable response of all symptoms to Lugol's solution and thyroidectomy is rapid and complete, as was shown in 10 cases. The 3 patients not operated on died, 2 of respiratory paralysis.

Although there is a close resemblance between thyrotoxic myopathy and progressive muscular atrophy, complete restoration of function and the disappearance of all signs under treatment militates against the presence of a disease of the central nervous system. Examination fails to show the neurologic signs associated with progressive muscular atrophy or amyotrophic lateral sclerosis. McEachern and Ross offer some evidence that the locus of weakness and fasciculation is at the myoneural junction, as follows: the patients complain of rapid loss of strength on action, as in myasthenia; Prostigmine abolishes weakness temporarily, as in myasthenia; and injection of the nerve with novocain does not stop the fasciculation of the appropriate muscle.

These authors refer to a case reported by Ayer, Means and Lerman.[42] This patient closely resembled others of the series analyzed by McEachern and Ross. He improved promptly following partial thyroidectomy and worked regularly for five years, when he developed pulmonary tuberculosis. Neurologic examination at that time was negative except for slight, fine tremor of the hands. The basal metabolic rate was –8 per cent, as against +60 per cent previously.

Another patient of this type was seen by me in 1939. He also recovered as a result of thyroidectomy, and was working as a mechanic more than two years afterward.

This disorder is undoubtedly rare, but should be recognized because of the fatal outcome that has been seen in untreated cases. With Lugol's solution and with thyroidectomy recovery is to be expected. As most patients present themselves within a few months of onset of weakness and rapidly progressive loss of weight, the illness should preferably be termed "acute" or "subacute."

Treatment of Carotid Aneurysm

The treatment of carotid aneurysm is an old topic, but recent papers make revision reasonable at the present time. The subject may be approached more intelligently if the following conclusions are admitted: Aneurysms of the brain are of common occurrence; for the most part they are untreatable by direct attack; but some, notably those involving the internal carotid arteries, can be successfully treated indirectly by surgery.

It may not be entirely sound on grounds of etiology or pathology to separate one type of aneurysm from another, but in most cases it is possible to state which are operable and which are not. Generally speaking, the commonest type of aneurysm is small, occurs especially at the junction of arteries composing the circle of Willis, and after an indefinite period may rupture spontaneously. Some authors think that these aneurysms arise from a congenital defect in the tunica elastica, but they have been found in many people well beyond youth or even middle age. When these miliary aneurysms rupture there is an outpouring of blood into the subarachnoid space, usually filling the basal cisterns and the spinal subarachnoid space, from which it is recovered by lumbar puncture. The symptoms are primarily those of an acute meningeal irritation. with or without focal cerebral or cranial-nerve signs. As a common site of this type of aneurysm is at the junction of the middle cerebral and posterior or anterior communicating arteries of the circle of Willis, the third nerve is often involved and pressure paralysis results. This location is nearly the same as that of saccular aneurysms, to be discussed later. Miliary aneurysms have been described by pathologists and clinicians in many papers during the past decade, and almost every physician will recognize this type

of aneurysm. Treatment is still a matter of debate, but no one has described a method of direct surgical intervention. Without specific treatment the outlook for recovery is good in approximately 50 per cent of cases.[43]

As contrasted with these minute aneurysms, there are the less frequent saccular ones. They are usually found in the large intracranial arteries, the basilar and internal carotid arteries in particular. That they have a different origin from miliary aneurysms is suggested by the fact that they do not commonly occur at arterial junctions, that they grow to a large size before rupturing, and that they are often associated with arteriosclerosis. One or two characteristics are held in common between miliary and saccular aneurysms. Neither seems to be caused by syphilis, and in neither do symptoms appear before rupture, so long as the saccular aneurysm remains small. But here the analogy ceases, for when a saccular aneurysm enlarges it does produce symptoms by pressure on neighboring structures; this is particularly true of the saccular aneurysms of the internal carotid artery, and in these surgery must be considered.

From the foregoing remarks, it appears that from the surgical therapeutic point of view the primary concern is with saccular aneurysms of the internal carotid artery in its intracranial course. The diagnosis can hardly be made until the aneurysm is large enough to produce pressure symptoms, and even then must be differentiated from tumors occupying the same site. If the patient or his physician hears a bruit, aneurysm is of course suggested, but a bruit is rare except in the case of arteriovenous aneurysms, which is not the subject of the present discussion. A favorite site for an expanding internal carotid artery is in its course at the border of the cavernous sinus, and in this region four cranial nerves are in immediate proximity, the third, fourth, fifth and sixth. Jefferson[44] has given clear-cut anatomical localization for this subclinoid type of carotid aneurysm, of which he found 16 in a series of 55 cases of intracerebral aneurysm. Utilizing the four cranial nerves mentioned, he localizes the site of aneurysmal dilatation in the three following categories:

Group A. Posterior Cavernous Syndrome. — Three divisions of trigeminus affected, with ocular palsies, sometimes only abducens; motor root of trigeminus usually affected, but may escape.

Group B. Middle Cavernous Syndrome. — First and second divisions of trigeminus affected, third spared; paralysis of one nerve, but usually of all nerves, supplying muscles of eye.

Group C. Anterior Cavernous Syndrome. — First division of trigeminus affected, other divisions spared; paralysis of superior division of the oculomotor nerve or of all nerves supplying muscles of eye.

It will be seen from the above schema that localization depends much on the amount of pressure exerted on the trigeminal roots.

Aneurysms may also develop in the internal carotid artery above the cavernous sinus and before the artery joins the circle of Willis. These supraclinoid aneurysms cause an entirely different compression syndrome from that of subclinoid aneurysms. In such a case the optic nerves, chiasm or optic tracts are pressed on, producing visual-field defects. Pituitary function may be disturbed so that an endocrine picture is presented similar to that of pituitary tumor. A number of such cases have been operated on and an aneurysm disclosed, to the embarrassment of the surgeon.[45, 46]

Objective aid in the diagnosis of carotid aneurysm may be obtained from x-ray examination of the skulls. The most significant findings are erosion of the clinoid processes of the sella turcica on the appropriate side and concentric calcification within the aneurysmal wall. Moreover, the aneurysm may be clearly delineated by thorotrast injection, as advocated by Moniz.[47]

Treatment should obviously be directed to reducing the size of the aneurysm or of doing away with it altogether. As the latter is technically impracticable one can only limit the amount of blood reaching the aneurysm, and for this Jefferson[44] offers three general procedures: occlusion of the common carotid artery, partial or complete ligature of the internal carotid artery in the neck and ligature of the carotid artery intracranially. He does not clearly commit himself concerning which procedure he favors, but one gathers in reading his papers that he is often satisfied with tying off the common carotid, which only partially reduces the blood reaching the brain via the internal carotid on the same side. Dandy[48] prefers to clip the vessel intracranially. It is a little difficult to estimate the value of these procedures, because the natural evolution of aneurysm appears to tend toward its occlusion, at least in some cases. Jefferson[44] describes such a case. Unexpectedly he uncovered an aneurysm in this location and withdrew; the patient recovered sufficiently to lead an active life for fourteen years. Seven years after the operation, x-ray examination suggested that the aneurysm was grossly calcified. Moreover, it is common knowledge that without ligation there may be no advance in symptoms over long periods of time, and since ligation seldom clears up existing symptoms, the results of a waiting policy and of ligation may be the same. If one could be sure that carotid ligation would prevent subsequent hemorrhage, this alone would be an indication for operation, but even this cannot be taken for granted.

Operative attack on the aneurysm itself is not recommended by anyone, although Dandy[49] was fortunate in removing a large aneurysm arising from the anterior cerebral artery, mistaken for tumor. When aneurysms have been opened through error the surgeon is usually pleased if he can retire without lethal bleeding.

Much has been said concerning the dangers of ligation of the internal carotid artery, and this subject has been carefully studied by Schorstein,[50] who collected 60 cases of aneurysm from the literature for statistical review. He divides them into three groups: infraclinoid (22 cases, no deaths); supraclinoid without leakage (22 cases, 3 deaths); and supraclinoid with leakage (12 cases, 5 deaths).

The principal complication following carotid ligation is hemiplegia, sometimes immediate and sometimes delayed. A variety of causes for such a serious complication have been entertained, namely, thrombosis by extension, embolism from a supposed thrombus distal to the ligature, and anoxemia from cutting off too much of the blood supply of the circle of Willis. Schorstein finds the evidence strongly in favor of simple ischemia, and concludes that it is the patency of the circle of Willis and general systemic blood pressure that determine whether or not ligation will lead to hemiplegia and death. Dandy[51] has performed 88 ligations of the internal carotid artery — partial ligation in the neck in 25 cases, total in the neck in 36 and intracranial clipping in 27. In all he observed immediate cerebral complications in 4 cases and late cerebral complications in 1 case, with 4 deaths. As a preventive he recommends the Matas procedure of intermittent digital compression of the carotid artery for two weeks prior to ligation, in order to improve collateral circulation through the circle of Willis.

It is difficult to summarize the subject because each case presents two unknown components of vital importance, that is, the exact size and condition of the aneurysm, and the patency of collateral circulation through the circle of Willis. If the latter is sufficient and if the general cardiovascular system is intact, ligation of the carotid artery, external or internal, is probably safe. Digital compression of the carotid should be used to check this. In selected cases, ligation can be expected to reduce the size of the aneurysm; in some cases it facilitates its obliteration and improves pressure symptoms, although seldom causing them to disappear. The above conclusions appear to be correct for all aneurysms of the internal carotid artery arising within the skull, but are especially applicable to those situated low, in or near the cavernous sinus.

Toxoplasmic Encephalitis

It is a question whether the practitioner of medicine will feel relieved at the recognition of another type of encephalitis. Time was when a case presenting acute cerebral symptoms of a diffuse character, in which bacteria could not be found or some poison could not be suspected, was labeled "toxic encephalopathy." In the last two decades, ever since the advent of the world-wide epidemic of acute encephalitis lethargica of 1917–1919, to be exact, considerable progress has been made, first in separating encephalitides from other types of cerebral lesions, such as vascular disease, tumor and abscess, and secondly in differentiating types of encephalitis. Yet even now it is difficult to define the term "encephalitis" or its associated spinal-cord term, "myelitis." Lest one think that the knowledge of the subject has made great strides, reference should be made to the paper of Adler,[52] who studied 100 cases in which there was a diagnosis of acute encephalitis. Because of autopsy findings or subsequent course the diagnosis had to be revised in 30! This was in 1940. Nevertheless, of the large and diverse group of diseases that are spoken of as primary encephalitis, Webster[53] was able to say in 1941 that nine types have thus far been shown to be due to viruses with a special predilection for the central nervous system. When one remembers the 1917–1919 epidemic, the epidemic of St. Louis encephalitis of 1933–1934 and the recent epidemic of equine encephalitis, one cannot help but be interested in the subject and greatly concerned for the future, for however much has been learned of the nature of the different viruses, there is as yet no planned treatment and only partial preventive measures, and wars and depressions are breeders of encephalitis.

The present section deals with another type of encephalitis, proved to be due to the protozoon Toxoplasma. During the last five years a series of papers have developed the knowledge of this disease, and now Cowen, Wolf and Paige[54] have assembled the cases and have described a distinct clinicopathological entity. From that article the following description of this disease is summarized.

The lesion is produced by the protozoon Toxoplasma, which is found in the cerebrum; it is associated with the formation of miliary granulomas with reactive gliosis and fibrosis, especially in the brain-cortex, basal-ganglia and periventricular areas. Large areas of necrosis result, which become calcified. The lesions have been found especially in young children and babies, and in 1 case a stillborn infant presented the full-blown picture of the disease, indicating that toxoplasmosis is congenital. Curiously enough, the mothers could

not be shown to be infected, although neutralization tests on their bloods were positive. Various mammals, and perhaps birds, are probably the animal reservoirs of the infection, but the mode of transmission to man is not yet known.

In these babies supposedly infected in utero, signs of the disease, such as ocular disturbances, notably strabismus and abnormal movements of the eyes, naturally appear early. In 8 patients, signs were seen during the first four days of life. Convulsions, focal or generalized, as well as hydrocephalus, were often early symptoms, and both of these persisted if the patient survived. Those living long enough presented mental retardation and behavior problems.

The most striking and frequent ocular signs were those observed in the eyegrounds. Of 11 patients examined ophthalmoscopically, 10 showed chorioretinal lesions, with pallor of the optic disks. Another constant sign was the demonstration by x-ray of calcium deposits, already mentioned as occurring in areas of necrosis in the brain, usually in multiple foci. The spinal fluid and the ventricular fluid were abnormal, both being xanthochromic and showing an increased number of cells, thought to be lymphocytes, and also elevated protein levels.

A number of symptoms and signs not referable to the nervous system were present, such as splenomegaly and hepatomegaly, vomiting, diarrhea and edema of the extremities. Blood and spinal fluid injected into mice and rabbits intracerebrally and intraperitoneally produced toxoplasmosis. Neutralizing antibodies could be demonstrated in the blood.

The authors quoted are concerned with infantile, probably congenital, toxoplasmosis, the subjects dying early or in childhood. Pinkerton and Weinman[55] describe a case in a man of twenty-two who ran an acute course and died on the twelfth day. Sabin[56] reports 2 children, six and eight years old, also with acute febrile illness, one dying and the other recovering. These 3 cases presumably represent a different — acquired — type of the disease. Finally, there is the report of two much older people, one fifty years of age, the other forty-three, who ran the course of an acute illness and died on the fifth day, the other on the twelfth. In one of these cases the parasites were demonstrated in focal areas of encephalitis, and inoculation of this material into guinea pigs and mice reproduced the disease.

Toxic Effects of Dilantin Sodium

Since its introduction as an anticonvulsant, Dilantin Sodium (sodium diphenyl-hydantoinate) has become one of the reliable drugs used in epilepsy, at least in this country. Toxic symptoms were described early in its use by Merritt and Putnam,[58] who introduced the drug into practice, and physicians are aware of most of these ill effects. Few have had the experience of Finkelman and Arieff,[59] who treated 44 patients with Dilantin and were forced to drop it in all except 7 cases because of toxic symptoms. They list thirty-one symptoms in all, the most commonly observed being ataxia, nystagmus, apprehensiveness and irritability, visual disturbances, tremors, electrocardiographic changes, nausea and vomiting, weight loss and gingivitis. They somewhat grudgingly admit that the 7 patients were continued on this treatment because they responded favorably to Dilantin when they had not done well under phenobarbital, bromides or both combined.

Rosenbaum[60] discusses this paper. He questions the implication that a number of the symptoms listed were due to Dilantin, and in particular he takes exception to the use of a paper published by him[61] as evidence of dangerous toxic effects of Dilantin. He had described a boy who took sixty to seventy capsules, or 6 to 7 gm., of phenytoin sodium in ten hours as a suicidal attempt. Severe toxic symptoms developed, but the patient recovered. Rosenbaum wrote, "The case thus illustrates the high safety factor of the drug," and concludes "The mild toxic symptoms encountered are well compensated by the striking and gratifying anticonvulsant action of the drug in many cases."

Still another case of acute poisoning from Dilantin is recorded by Robinson.[62] His patient took 4.5 gm. at one dose and recovered. Incidentally, a week later he was continued on Dilantin, 0.1 gm. three times daily, and "when seen six weeks later he showed no unusual sequelae."

It would seem that Dilantin Sodium has passed the experimental phase and found a definite place in the treatment of epilepsy, in spite of toxic symptoms. Its margin of safety as judged by acute poisoning appears to be considerable.

References

1. National Research Council. Chemotherapy for infectious diseases and other infections. *J. A. M. A.* 116:513-517, 1941.
2. Dingle, J. H., Thomas, L., and Morton, A. R. Treatment of meningococcic meningitis and meningococcemia with sulfadiazine. *J. A. M. A.* 116:2666-2668, 1941.
3. Finland, M., Strauss, E., and Peterson, O. L. Sulfadiazine: therapeutic evaluation and toxic effects on four hundred and forty-six patients. *J. A. M. A.* 116:2641-2647, 1941.
4. Finland, M., Peterson, O. L., and Goodwin, R. A., Jr. Sulfadiazine: further clinical studies of its efficacy and toxic effects in four hundred and sixty patients. *Ann. Int. Med.* 17:920-934, 1942.
5. Janeway, C. A. The sulfonamides. *New Eng. J. Med.* 227:989-995 and 1029-1044, 1942.
6. Case records of the Massachusetts General Hospital (Case 28501). *New Eng. J. Med.* 227:922-927, 1942.
7. Bieter, R. N., Baker, A. B., Beaton, J. G., Shaffer, J. M., Seery, T. M., and Orr, B. A. Nervous injury produced by sulfanilamide. *J. A. M. A.* 116:2231-2236, 1941.
8. Tolosa, A., and Savoy, C. V. Sobre um caso de polineurite sulfamidica. *Sao Paulo Med.* 12:269-279, 1939.
9. Ornsteen, A. M., and Fürst, W. Peripheral neuritis due to sulfanilamide. *J. A. M. A.* 111:2103, 1938.

10. Elkington, J. St. C. **Peripheral nerve palsies following intramuscular injection of sulphonamides.** *Lancet* **243:425, 1942.**

11. Johnstone, D. F., and Forgacs, P. **Cerebral symptoms occurring during sulphapyridine treatment of meningococcal meningitis.** *Brit. M. J.* 1:772-774, 1941.

12. Roseman, E., and Aring, C. D. **Encephalopathy associated with sulfamethylthiazole therapy.** *New Eng. J. Med.* **224:416-420, 1941.**

13. Blankstein, S. S. **Transitory myopia: complication of sulfanilamide therapy.** *Am. J. Ophth.* **24:895-899, 1941.**

14. Little, S. C. Nervous and mental effects of sulfonamides. *J. A. M. A.* 119:467-474, 1942.

15. Wegeforth, P., and Essick, C. R. **Effect of subarachnoid injections of antiseptics on central nervous system.** *J. Pharmacol. & Exper. Therap.* 13:335-354, 1919.

16. Watt, A. C., and Alexander, G. L. **Epilepsy following application of sulphathiazole near brain.** *Lancet* **1:493-495, 1942.**

17. Pilcher, C., Angelucci, R., and Meacham, W. F. Convulsions produced by intracranial implantation of sulfathiazole. *J. A. M. A.* **119:927,** 1942.

18. Hurteau, E. F. Intracranial use of sulphonamides: experimental study of histology and rate of absorption. *Canad. M. A. J.* **44:352-355,** 1941.

19. *Idem.* Intracranial use of sulfadiazine: experimental study of histology and rate of absorption. *Canad. M. A. J.* **46:15-17,** 1942.

20. Ingraham, F. D., and Alexander, E., Jr. **Experimental application of sulfonamide drugs to cerebral cortex.** *New Eng. J. Med.* **227:374-378,** 1942.

21. Blalock, A., Harvey, A. McG., Ford, F. R., and Lilienthal, J. L., Jr. Treatment of myasthenia gravis by removal of thymus gland. *J. A. M. A.* 117:1529-1533, 1941.

22. Poer, D. H. Effect of removal of malignant thymic tumor in case of myasthenia gravis. *Ann. Surg.* **115:586-595, 1942.**

23. Blalock, A., Mason, M. F., Morgan, H. J., and Riven, S. S. Myasthenia gravis and tumors of thymic region. *Ann. Surg.* **110:544-561,** 1939.

24. Campbell, E., Fradkin, N. F., and Lipitz, B. Myasthenia gravis treated by excision of thymic tumor. *Arch. Neurol. & Psychiat.* 47:645-661, 1942.

25. Turnbull, F. Removal of malignant thymoma in case of myasthenia gravis. *Arch. Neurol. & Psychiat.* **48:938-945, 1942.**

26. Viets, H. R. Personal communication.

27. Mella, H. Irradiation of thymus in myasthenia gravis. *M. Clin. North America* 7:939-949, 1923.

28. Viets, H. R., Schwab, R. S., and Brazier, M. A. B. Effect of pregnancy on course of myasthenia gravis. *J. A. M. A.* **119:236-242,** 1942.

29. Strickroot, F. L., Schaeffer, R. L., and Bergo, H. L. Myasthenia gravis occurring in infant born of myasthenic mother. *J. A. M. A.* **120:1207-1209,** 1942.

30. Lieberman, A. T. Myasthenia gravis with acute fulminating onset in child five years old. *J. A. M. A.* **120:1209-1211, 1942.**

31. Riley, H. A., and Frocht, M. Myasthenia gravis: incidence in two sisters. *Proc. Am. Neurol. Soc.* **68:100-102, 1942.**

32. Schwab, R. S., and Viets, H. R. Prostigmin test in myasthenia gravis. *New Eng. J. Med.* **219:226-228,** 1938.

33. King, A. B., and Ford, F. R. Clinical and anatomical study of neurological conditions resulting from metastases in central nervous system due to carcinoma of lung. *Bull. Johns Hopkins Hosp.* **70:124-156,** 1942.

34. Globus, J. H., and Meltzer, T. Metastatic tumors of brain. *Arch. Neurol. & Psychiat.* 48:163-226, 1942.

35. Quinby, W. C. Carcinoma of prostate. *New Eng. J. Med.* **227:512-515,** 1942.

36. Huggins, C., Stevens, R. E., and Hodges, C. V. Studies on prostatic cancer: effects of castration on advanced carcinoma of prostate gland. *Arch. Surg.* **43:209-223,** 1941.

37. Alyea, E. P., and Henderson, A. F. Carcinoma of prostate: immediate response to bilateral orchidectomy: clinical and x-ray evidence. *J. A. M. A.* **120:1099-1102,** 1942.

38. Chute, R., Willetts, A. T., and Gens, J. P. Experiences in treatment of carcinoma of prostate with stilbestrol and with castration by techinque of intra-capsular orchidectomy. *J. Urol.* **48:682-692,** 1942.

39. Nesbit, R. M., and Cummings, R. H. Prostatic carcinoma treated by orchidectomy. *J. A. M. A.* **120:1109-1111,** 1942.

40. Clarke, B. G., and Viets, H. R. Effect of diethylstilbestrol on neurologic symptoms of carcinoma of prostate. *J. A. M. A.* **121:499-501,** 1943.

41. McEachern, D., and Ross, W. D. Chronic thyrotoxic myopathy. *Brain* **65:181-192,** 1942.

42. Ayer, J. B., Means, J. H., and Lerman, J. Simulation of progressive muscular atrophy by exophthalmic goiter. *Endocrinology* **18:701-704,** 1934.

43. Richardson, J. C., and Hyland, H. H. Intracranial aneurysms. *Medicine* **20:1-83,** 1941.

44. Jefferson, G. On saccular aneurysms of internal carotid artery in cavernous sinus. *Brit. J. Surg.* **26:267-302,** 1938.

45. *Idem.* Compression of chiasma, optic nerves, and optic tracts by intracranial aneurysms. *Brain* **60:444-497,** 1937.

46. Klemme, R. M., and Woolsey, R. D. Suprasellar aneurysm. *Arch. Neurol. & Psychiat.* **47:662-666,** 1942.

47. Moniz, E. *Angiographie cerebrale ses applications et resultats en anatomie physiologie et clinique.* 327 pp. Paris: Masson et Cie, 1934.

48. Dandy, W. E. Intracranial arterial aneurysms in carotid canal. *Arch. Surg.* **45:335-350,** 1942.

49. *Idem.* Aneurysm of anterior cerebral artery. *J. A. M. A.* **119:1253,** 1942.

50. Schorstein, J. Carotid ligation in saccular intracranial aneurysms. *Brit. J. Surg.* **28:50-70,** 1940.

51. Dandy, W. E. Results following ligation of internal carotid artery. *Arch. Surg.* **45:521-533,** 1942.

52. Adler, A. One hundred cases of condition diagnosed as acute encephalitis. *Arch. Neurol. & Psychiat.* **44:541-567,** 1940.

53. Webster, L. T. Classification of primary encephalitides of man according to virus etiology. *J. A. M. A.* **116:2840,** 1941.

54. Cowen, D., Wolf, A., and Paige, B. H. Toxoplasmic encephalomyelitis: clinical diagnosis of infantile or congenital toxoplasmosis; survival beyond infancy. *Arch. Neurol. & Psychiat.* **48:689-739,** 1942.

55. Pinkerton, H., and Weinman, D. Toxoplasma infection in man. *Arch. Path.* **30:374-392,** 1940.

56. Sabin, A. B. Toxoplasmic encephalitis in children. *J. A. M. A.* **119:801-807, 1941.**

57. Pinkerton, H., and Henderson, R. G. Adult toxoplasmosis. *J. A. M. A.* **116:807-814,** 1941.

58. Merritt, H. H., and Putnam, T. J. Sodium diphenyl hydantoinate in treatment of convulsive seizures: toxic symptoms and their prevention. *Arch. Neurol. & Psychiat.* **42:1053-1058,** 1939.

59. Finkelman, I., and Arieff, A. J. Untoward effects of phenytoin sodium in epilepsy. *J. A. M. A.* **118:1209-1212,** 1942.

60. Rosenbaum, M. Toxic effects of phenytoin sodium. *J. A. M. A.* **119:582, 1942.**

61. *Idem.* Ingestion of large doses of dilantin sodium. *Arch. Neurol. & Psychiat.* **45:265-270,** 1941.

62. Robinson, L. J. Case of acute poisoning from dilantin sodium with recovery. *J. A. M. A.* **115:289,** 1940.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29131

PRESENTATION OF CASE

A fifty-nine-year-old Russian restaurant porter came to the hospital because of abdominal fullness, anorexia and loss of weight.

The patient apparently was well until two months before entry, when he developed constipation, which was relieved by saline purgatives. Occasionally his stools were black, but at no time were they bloody or acholic. Six weeks before admission, his appetite began to fail and his diet consisted largely of soups, cake, milk and fruit. One week later he began to suffer with a "burning feeling" in the upper abdomen, which was associated with frequent belching and was unrelated to meals or any particular food. Soon after this his urine became "brown, like tea" and he developed nocturia (ten or twelve times). Occasionally, in the morning he had shaking chills, which were followed by drenching sweats. About the same time he noted a nontender mass in the upper abdomen. Ten days before entry his ankles became swollen. There was no diarrhea, vomiting, jaundice, dyspnea, orthopnea, anginal pain, palpitation, flank pain, hesitancy, dribbling, dysuria or hematuria. He had lost 40 pounds of weight during the year previous to admission.

The family history was noncontributory. The patient was born in Russia but had lived in Massachusetts for forty-two years. He had worked in an iron foundry and a cloth mill, and more recently had been a porter in a restaurant. His diet was said to have been good prior to the present illness. Since the age of twenty-one he drank one or two glassfuls of beer or jiggers of whiskey daily, but he had had neither during the six months prior to admission. He denied having had rheumatic, typhoid or typhus fever or malaria.

Physical examination disclosed a pale, wasted man who was slightly dyspneic on exertion. The chest was barrel shaped and hyper-resonant. The examination of the heart and lungs was negative. The abdomen was markedly protuberant and the skin seemed tense. In the upper abdomen there was a firm, smooth, nontender mass extending to the umbilicus. The mass moved with respirations and seemed to be a part of the liver. The spleen was easily palpable and seemed extremely large. No ankle edema was demonstrated.

The blood pressure was 95 systolic, 40 diastolic. The temperature was 97.9°F., the pulse 65, and the respirations 20.

The examination of the blood revealed a red-cell count of 3,160,000 with a hemoglobin of 55 per cent and a white-cell count of 6800 with 68 per cent polymorphonuclear leukocytes, 28 per cent lymphocytes, 2 per cent monocytes and 2 per cent eosinophils. The urine was acid in reaction. On three occasions it showed a + or ++ test for albumin; the test was negative in nine examinations. In three examinations of a total of twelve, the urine was slightly positive for bile. The sediment occasionally contained a small number of white cells. The stool was guaiac positive once in seven examinations. The blood Hinton test was negative. The serum protein was 5.1 gm., the albumin 2.3 gm., the globulin 2.8 gm., and the nonprotein nitrogen 28 mg. per 100 cc.; the bicarbonate was 22.5 milliequiv., and the chloride 99.3 milliequiv. per liter. The cephalin flocculation test was negative. The prothrombin time was 33 seconds (normal, 20 seconds). A Congo red test showed 33 per cent retention of the dye in the serum; 2.12 gm. of hippuric acid was excreted in the urine in four hours (5.9 gm. of sodium benzoate was administered by mouth). An intradermal skin test with echinococcal antigen was negative. An electrocardiogram was not remarkable.

A flat film of the abdomen showed a small liver and an enlarged spleen. There was a single round opaque shadow in the right upper quadrant outside the kidney shadow that suggested a gallstone. The kidneys seemed normal in the intravenous pyelograms. In a chest roentgenogram the right costophrenic angle was obliterated, probably by adhesions. The lung fields were not remarkable. No esophageal varices were seen after a barium meal. The stomach appeared normal. A large mass lay above the stomach and could be separated from it. The mucosal markings of the stomach were normal, as was the duodenal loop. A barium enema showed that the transverse colon was depressed by a large midline mass; no other abnormality was demonstrated. Films of the long bones and pelvis and a lateral view of the skull showed no evidence of disease.

The patient did not respond to a high-vitamin, high-carbohydrate and low-fat diet, and the blood prothrombin time remained prolonged in spite of large doses of parenterally administered vitamin K.

A peritoneoscopy was performed on the eighteenth hospital day.

Differential Diagnosis

Dr. Wyman Richardson: We are confronted with a patient who showed definite evidence of impaired liver function and a large upper abdominal mass. In the first place I shall review the evidence for failure of liver function.

The total protein was somewhat low and the globulin was greater than the albumin. That may be evidence of liver failure. The hippuric acid test was on the low side, definitely below what is usually accepted as normal.

Let us consider the prothrombin time, which I think is helpful in intrinsic liver disease. It was definitely prolonged and remained so in spite of what we may presume was adequate parenteral dosage of vitamin K. I think that is definite evidence of intrinsic liver disease — liver failure. There is some question of the absence of bile in the stool from the story, but if the increased prothrombin time was due to lack of bile salts it should have responded to vitamin K therapy. The anemia is consistent with liver failure but not specific for it. It is curious that, although they did a cephalin flocculation test, which was negative, there was no attempt to measure the blood bilirubin, which might be of some help. We can assume there was increase in blood bilirubin if the urine test was positive for bile. I assume that it was, since it is so stated, definitely, on three occasions. I think I may be getting more fussy as the years roll by, but I spend a lot of time talking to the second-year students on the value of looking at a stool, and in this case I should rather know what it looked like than to know it was guaiac positive. It is fair to assume it was normal in color. Thus, there is evidence of impaired function of the liver — evidence that is consistent with cirrhosis of the liver.

Against the diagnosis of cirrhosis of the liver are the absence of esophageal varices, the negative cephalin flocculation test — if you believe in it — and a clinical course that seems more rapid than that in the ordinary type of cirrhosis of the liver.

Let us turn to the abdominal mass. Clinically it was in the upper abdomen, in the midline, moved with respiration, and was thought to be attached to the liver. By x-ray the mass was said to have been above the stomach; whether that means cephalad or anterior, I do not know.

Dr. George W. Holmes: It means cephalad.

Dr. Richardson: And if it displaced the transverse colon, it probably displaced the stomach too. Perhaps we might look at the plates.

Dr. Holmes: In the chest film the lung fields are negative except for this obliteration of the angle between the diaphragm and the chest wall, low down on the right; I should say that it is negative for anything that has any bearing on the symptomatology in this case. The heart is somewhat enlarged, and the vessels perhaps a little prominent. What could produce such an appearance as that? Of course, an inflammatory process, either just above or below the diaphragm might result in such an appearance, or it could be in some way connected with this mass, which we see below the diaphragm on the left side. In the oblique view the angle between the chest wall and diaphragm is obliterated in front. I do not believe that is of importance. In this film you see the mass that has been described.

Dr. Richardson: On which side.

Dr. Holmes: On the left side. This is the cecum.

Dr. Richardson: And this shadow was thought to be spleen?

Dr. Holmes: Yes; enlarged spleen, I suppose.

There is a pressure defect in the upper portion of the stomach. The kidneys were studied in an attempt to rule them out as part of the mass; I should say that they are normal. The outline of the liver is indefinite, but the organ is small rather than large. The fact that these films do not show varices does not prove that they were not there; even with a careful examination they are sometimes missed.

Dr. Richardson: Does the gallstone show here?

Dr. Holmes: I do not see it.

Dr. Richardson: What was the mass? I do not believe it was due to an infectious process. There is a history of fever before entry to the hospital, with chills and drenching sweats, but it does not appear to have been prominent during his stay in the hospital. The blood picture is against a pyogenic infection, but of course it is consistent with some other type of infection. Nor do I see any good reason for talking about such things as echinococcal cyst, which usually has a much longer course than this and does not result in such serious symptoms so quickly.

I do not see any good reason to doubt that this was some type of tumor. A tumor in this region that produces this degree of displacement is difficult for me to explain unless it actually involves the liver. I cannot conceive of its being pancreas. It was said to move with respiration. One can consider various types of cysts and so forth, but the whole impression is that of a rapidly progressive disease. I asked about the gallstone because of the question whether one should consider biliary-tract carcinoma superimposed on an old chronically inflamed gall bladder with stones, and I think one should have that in mind. My impression is that this is a tumor. If it is a tumor, and if it involves the liver, we have no evidence of

its primary source. Having built up a case that is consistent with intrinsic liver disease — and I might say parenthetically that such a condition could explain the enlargement of the spleen — on the basis of a cirrhotic liver, one is justified in considering a diagnosis of primary liver tumor or hepatoma. The only difficulty with this diagnosis is that the tumor seems to have extended far down in the abdomen. However, it might have been on the under surface of the left lobe. I still think it was a liver tumor.

I conclude that the patient had underlying liver failure, probably portal cirrhosis of the liver, and that there was a tumor in the abdomen, probably a primary tumor of the liver, otherwise known as hepatoma.

In every case that one sees in medicine there is some mystery. The mystery in this case is, Why did anyone do a Congo red test? It was done, and if I interpret these findings correctly it was positive according to the criteria of some observers; 67 per cent of the dye was removed from the serum, which I think some members of the Arthritic Service would say was definite evidence of amyloid disease. My experience on the Medical Service is that amyloid disease is extremely rare. I cannot see how to fit it into this problem. I do not recognize a condition of localized amyloidosis that would cause a local tumor limited to the liver.

Another thing that bothered me is that the person who abstracted this record made a great effort to make it clear that there was no real evidence of nephrosis in the urine. There was albumin on only one or two occasions, and the suggestion seems to be that there should have been more albumin. However, in spite of all the things about amyloid disease, I do not believe that one can count on a Congo red test to make a diagnosis. This patient did not have amyloidosis, either from the clinical picture or from the physical or x-ray findings. If it was present I am sure it was purely incidental.

There is one further point in regard to the anemia: it could have been due to cirrhosis of the liver, but it also could have been due merely to malnutrition and lack of some of the factors necessary for blood formation.

My final diagnoses are portal cirrhosis of the liver and primary tumor of the liver.

Dr. Chester M. Jones: I suggest that Dr. Holmes be asked whether the left lobe of the liver was enlarged, even though it looks small, and the x-ray report stated that there was a "small liver." With the displacement of the stomach it looks as if the left lobe might have been large.

Dr. Holmes: I agree that there is a mass in the region of the left lobe of the liver; whether it is an unusually shaped liver or a tumor, I do not know.

Dr. J. H. Means: This case puzzled us enormously, and I should like to congratulate Dr. Richardson on his excellent handling of it. The abstract oversimplifies the situation by including the x-ray findings and not the peritoneoscopic findings, which were at variance. The radiologists thought the liver was small, and the endoscopist thought it was large. I think we should have been a great deal better off if we had not had so much expert advice.

We knew the patient had a "sick liver." That was obvious enough, but we thought he must have something else, just as Dr. Richardson did. What I felt in the abdomen was rather odd. I made out a huge organ with an edge. Whether it was liver or liver plus spleen, I was not certain. The outline was rather queer for liver. It went in the wrong direction on the right side. In other words, it went from northwest to southeast, and then made an angle and went up in a northeasterly direction from below the umbilicus. I was gratified that the autopsy findings disclosed that that was a fairly correct description of what was present.

I am rising to the defense of the Congo red test — I asked for it. There are several points in common between this case and that of a colored girl we had seen eight months earlier. She had a huge liver and spleen and ran a fever very much like this man's. We did a Congo red test and found that she took up all the dye. It was positive on two occasions. Then we got Dr. Benedict to look in. We hoped that he would find some organ stained red with the dye, but he could not do so. Because the cases had points of similarity I thought it would be interesting to do a Congo red test on this man. He had a positive one, but I do not know how to interpret it. That is as far as we got. We treated him for the sick liver, which we knew he had. He was reluctant to let us give intravenous injections and finally rebelled completely, when he went steadily downhill and died.

Should we not hear from the endoscopist?

Dr. Edwin B. Benedict: There was no tumor. The liver and the spleen were enlarged — two separate masses, with fluid in the abdomen. Also, I should like to rise to the defense of the endoscopist, because I think his findings proved to be more accurate than those of the radiologist.

Clinical Diagnosis

Lymphoma, with metastases to spleen?
Gaucher's disease ??

Dr. Richardson's Diagnoses

Portal cirrhosis of liver.
Primary tumor of liver (hepatoma).

Anatomical Diagnoses

Subacute hepatitis, with diffuse cirrhosis (? syphilitic).
Ascites.
Splenomegaly, slight.
Cholecystitis, chronic.
Cholelithiasis.
Arteriosclerosis, moderate.

Pathological Discussion

Dr. Tracy B. Mallory: As I read over this history I made the same diagnosis as Dr. Richardson did, which is wrong. I am not quite so sure what the correct diagnosis is.

The liver weighed 2300 gm. The enlargement, however, was almost entirely in the left lobe, the right lobe having shrunken. As a result the liver had pivoted on its suspensory ligament, and its edge ran diagonally across the abdomen in the wrong direction, as Dr. Means has described in mariner's terms. The spleen was moderately enlarged. There were some questionable varices in the esophagus, which were not extremely impressive. No tumor was found. The mass was the hypertrophied left lobe of the liver. The organ as a whole was very finely granular, and except for the disproportion of size, the two lobes were similar.

On microscopic examination it shows an extremely diffuse fibrosis, which not merely encapsulates lobules and nodules of liver tissue but invades every lobule. The distribution of fibrous tissue is much like that of amyloid deposits in the liver; the liver tissue, however, failed to give a positive amyloid reaction. There also is an active progressive hepatitis, with monocytes and lymphocytes predominating in the infiltrate. If I saw this microscopic picture in a child I should have no hesitancy in saying it was congenital syphilis of the diffuse type. Most textbooks of pathology say that diffuse syphilis of the liver, though extremely rare, may occur in an adult. Dr. Alexander J. Michie reminded me of McCrae's* paper on syphilis of the liver. That is a purely clinical study, but this case fits well and the fever is characteristic. Involvement of the left lobe has apparently been noted in more than half the cases. Negative serologic tests are said to be not extremely unusual, although, of course, McCrae's paper was written before the days of precipitation tests, when one had to rely exclusively on the Wassermann test. The demonstration of spirochetes could settle the diagnosis, but our efforts to date have proved fruitless.

Dr. Jacob Lerman: On rounds we discussed the possibility of the left-lobe enlargement's being due to syphilis, but we placed a lot of emphasis on the negative Hinton test and therefore ruled it out.

Dr. Mallory: It is too bad that we did not repeat the serologic test using dilutions of the serum. The serum from a patient of this sort might have such an extremely high titer that it would give a prezone phenomenon.

Dr. Richardson: What happened to the red dye?

Dr. Mallory: We found none of it.

*McCrae, T., and Caven, W. R. Tertiary syphilis of liver. *Am. J. M. Sc.* 172:781-796, 1926.

CASE 29132

Presentation of Case

A twenty-seven-year-old married dentist was referred to the hospital because of fever and a persistent nonproductive cough of six weeks' duration.

The patient had always been in excellent health until three months before admission when during the summer, without known precipitating factors, he experienced a sharp pain that began in the right shoulder but soon settled in the anterior right chest. This was made worse by deep respirations and movements of the trunk. Six weeks before admission he suddenly developed a nonproductive irritating cough but did not have an upper respiratory infection. This continued to the day of admission without any change in severity and did not respond to cough medicine prescribed by his physician. Two weeks before entry the physician found that the patient's temperature was 100.2°F., the pulse 120, and the respirations 30. Chest films at another Boston hospital were said to have revealed "a mass in the right lung that was cystic and contained fluid." During the week prior to admission he had a daily temperature elevation to 101°F. and drenching night sweats. There was no hemoptysis, weight loss, palpitation, dyspnea, chills or cyanosis.

The family history was noncontributory. The patient was born in Boston and had lived there most of his life.

Physical examination disclosed a well-developed and well-nourished man in no apparent distress. The trachea was in the midline; the chest seemed symmetrical, but there was some lag in expansion on the right. There were dullness and diminished breath sounds on the right side to the level of the eighth rib posteriorly and the clavicle anteriorly. Scattered crackling rales and bronchovesicular breathing were audible in the midscapular region. Examination of the left lung, heart and abdomen was normal. There was minimal clubbing of the fingers.

The blood pressure was 130 systolic, 82 diastolic. The temperature was 98.6°F., the pulse 120, and

the respirations 35. The pulse and respirations remained rapid throughout hospitalization. The temperature rose to 100.4°F. on the fourth hospital day and subsequently varied between normal and 102°, but did not rise in abrupt sharp peaks.

The hemoglobin was 12 gm. per 100 cc., and the white-cell count 16,900. The urine was acid in reaction and had a specific gravity of 1.020; the sediment contained rare red and white cells. The blood Hinton test was negative.

A chest roentgenogram disclosed a 12 by 15 cm. smooth, homogeneous mass that filled the anterior two thirds of the lower right chest and rose to the level of the second rib anteriorly. The mass appeared to arise from the anterior mediastinum on the right side. The right main bronchus and its subdivisions were not grossly abnormal. There was a small amount of fluid in the right pleural space. The left lung field was clear; the heart was not definitely abnormal and the left diaphragmatic shadow appeared normal. There was no evidence of mediastinal shift or of definite esophageal displacement.

An operation was performed on the ninth hospital day.

Differential Diagnosis

Dr. Austin Brues: I have culled briefly the significant points in this short report. We have a twenty-seven-year-old dentist who, for three months, had anterior chest pain heralded in by shoulder pain, pleural in type, which was increased by respirations and by movements of the trunk. Six weeks before entry he developed a cough, which apparently was never productive. Four weeks later, fever was first noted, which was of a mildly septic type. After that he had tachycardia and rapid breathing, but no general prostration. There was a mild anemia, and a minimal clubbing of the fingers; physical and x-ray examinations agree in the mass in the right anterior chest coalescent with the mediastinum, with a small amount of pleural fluid on that side. There are also two collateral observations that I should like to bring up. First the outside x-ray films which, using legal terminology, we might call "hearsay evidence," which may be important. The description given us is that of a cyst containing some fluid, and we should suspect that such a definite description would have been made only if a fluid level had been observed. We therefore have hearsay evidence that, at that time, instead of a solid lesion there was one which was thought to contain fluid and perhaps had a fluid level. The second collateral observation we may class in accordance with our legal analogy as "circumstantial evidence": an operation was performed. The operation must have revealed something of sufficient significance to the Pathology Department to make it the subject of a clinicopathological conference. In other words, something more than pus must have been found.

One bit of evidence that is lacking is a blood smear. Perhaps it was not made. It might encourage or discourage certain diagnoses that I think for other reasons are improbable — namely, tuberculosis, in which the granulocytes are relatively low and the monocytes high; parasitic disease, which is usually accompanied by an eosinophilia; Hodgkin's disease, which often shows a high granulocyte count and possibly eosinophilia; and leukemia, in which a smear may give obvious evidence of the condition.

Dr. Tracy B. Mallory: The white-cell count was 12,400, with 79 polymorphonuclear leukocytes, 11 small lymphocytes, 8 monocytes and 2 eosinophils. The red cells and platelets appeared normal.

Dr. Brues: We have a process limited to the right chest with initial pain suggesting pleural involvement. I do not believe there was massive pleural involvement, such as we might expect with an endothelioma of the pleura, because of the small amount of fluid that is reported. We do however expect to find something encroaching on the pleura and giving the first symptom in that way.

I should like next to consider fever as a symptom. This suggests primary infection, some lesion secondarily infected or a series of other conditions that might be febrile, such as Hodgkin's disease, sarcoid and metastatic disease; of the latter, Ewing's tumor is the only commonly febrile representative and is out of the question without evidence of a primary lesion. I shall pass over sarcoid, and say in connection with Hodgkin's disease that the reported nonlobulated configuration of the growth, the fact that pain was the first symptom and occurred long before the others, and the fact, if true, that a fluid level was seen are against the diagnosis. Furthermore, fever in Hodgkin's disease is usually observed either in advanced cases or in cases with posterior rather than anterior mediastinal involvement.

It might be appropriate to take up the x-ray films at this point.

Dr. George W. Holmes: The films that I have put up cover a period of about three months. They show a very large mass that occupies the midchest. In the anteroposterior view it is in the central portion of the chest. In the lateral view it also appears to be in the midportion rather than in the front or back. It is of some interest that a mass as large as that does not displace the heart. We might assume that the lung was collapsed behind it, so that we do not see it, and that one compensates the other and there is no displacement. There

is evidence in this film of a small amount of fluid in the pleural space. The mass is homogeneous, with sharply defined borders, and is not lobular.

DR. BRUES: Does this exhibit include the plate taken in the outside hospital on which I was speculating?

DR. HOLMES: No. Of course that would be of great value.

In the spine the fifth lumbar vertebra has a narrow posterior portion. I do not believe that this represents metastatic malignancy.

DR. BRUES: We must still consider primary infections and secondarily infected processes. I shall first mention the possible primary infections. There was no history of pneumonia, and the x-ray films do not suggest that the lesion was of that type. The course was not septic enough to suggest a large encapsulated empyema, and I suspect that the rounded lower border of the mass by x-ray makes an interlobar accumulation of fluid or pus unlikely.

Tuberculosis, of course, is suggested by the first few lines in the record. The significant point against tuberculosis is the absence of disease in the apices. One might also think of two other processes similar to tuberculosis but without the same tendency to occur in the apices — actinomycosis and streptothricosis. Either of these, however, should give greater prostration.

An amebic abscess working its way up from the liver is indicated in the beginning of the history since the pain occurred in the shoulder, suggesting something in the region of the diaphragm. One might think of an amebic process passing from the liver through the diaphragm, settling in the lung and giving these symptoms. Again, one would expect considerable prostration.

Against echinococcal disease is the fact that the patient was apparently a confirmed Bostonian.

Did he have a lung abscess? Such a process would have been walled off rather thoroughly, since there was no sputum, which is strongly against the diagnosis. Furthermore, the x-ray films show no particularly marked degree of infiltration around the process.

The fact that the fever occurred late suggests a secondary process. Cancer of the lung, centrally located, can be walled off so that no sputum appears, but this is unusual. The patient was young for cancer to occur, but not too young. In its favor is the lack of displacement of the mediastinum, such as may occur in an infiltrative lesion. Against it, for the same reason, is the absence of infiltration in other directions.

Two other processes start early in life and give their peak incidences of trouble in the third decade, namely, congenital cystic disease and dermoid cyst. Both of these may show a fluid level at some time. Dermoids are particularly likely to occur in the anterior part of the chest coalescing with the mediastinal shadow and appearing low in the lung fields. One would expect a dermoid to displace the mediastinum to the opposite side, and that worried me somewhat, but I was inclined to pass that off, and Dr. Holmes has given me assistance in doing so. Therefore, because of the age, the location, the recent febrile course, the absence of sputum and the lack of definite evidence against it, I shall make the diagnosis of dermoid cyst, secondarily infected.

DR. MALLORY: What was the line of argument before operation, Dr. Brown?

DR. ROBERT K. BROWN: We thought the lesion probably was a dermoid cyst. The patient was extremely sick when he came in. His pulse is recorded at 120, but it ranged from 120 to 140 and did not go down after a week's rest in bed. The temperature went up and ranged from 100 to 102°F., not a definite septic temperature. Dr. Churchill thought that the patient was not in condition for open thoracotomy such as would be required in an attempt to remove the whole lesion, and decided merely to explore under local anesthesia through an anterior incision.

DR. MALLORY: I think you might as well go ahead and tell the operative findings.

DR. HOLMES: May I say a word first? If you arrive at a diagnosis of cyst there are some points in the x-ray examination that may help to decide between dermoid and other forms of cyst. For instance, an echinococcal cyst usually has calcified walls, and a dermoid cyst often shows variations in density within the cyst itself, such as teeth and areas of markedly diminished density due to fat. Although the latter may also look just like this one, the absence of variations in density is perhaps against it.

DR. RICHARD SWEET: I have just taken a dermoid cyst out of a mediastinum that showed marked calcification in the wall.

CLINICAL DIAGNOSIS

Dermoid cyst.

DR. BRUES'S DIAGNOSIS

Dermoid cyst, secondarily infected.

ANATOMICAL DIAGNOSES

Teratoma of mediastinum, with extension to middle lobe of right lung and metastases to liver and vertebras.
Pathologic fracture of fifth lumbar vertebra.
Collapse of right lung, massive.
Bronchopneumonia, slight, of left lung.
Ascites.
Operative wound: exploratory thoracotomy.

Pathological Discussion

Dr. Mallory: Will you tell us the operative findings, Dr. Brown?

Dr. Brown: A large mass was found with a solid wall about 1 cm. thick and a necrotic center consisting of gray mushy material.

Dr. Mallory: A biopsy specimen showed a tumor which in part appeared to be carcinomatous with some rather poorly formed glands, which were enough to justify one in thinking of it as adenocarcinoma. Other portions of the tumor were composed of long spindle cells that looked fibroblastic. We thought we were probably justified in assuming that there were two kinds of cells and that this was therefore an undifferentiated teratoma rather than a carcinoma. Following that, x-ray treatment was given. Dr. Brown will tell the rest of the story.

Dr. Brown: The lesion did not change with 1,000,000-volt x-ray therapy, even in large dosage. In two months he came in again with a pathologic fracture of the fifth lumbar vertebra, which was treated by x-ray; the patient was put in a plaster shell. Two months later he came back terminally, with a large liver and ascites; he died in six days.

Dr. Mallory: At post-mortem examination we found a large tumor in the anterior mediastinum projecting into the pleural cavity. It was very firm and was adherent to the middle lobe of the right lung, and on section it was possible to show that it had invaded the middle lobe. That left two possibilities — it was either a mediastinal teratoma with secondary invasion of the lungs or a primary carcinoma of the lung spreading into the mediastinum. It seemed to us from gross examination that the latter was unlikely since the tumor was largely at the periphery of the lung and the bronchi were entirely uninvolved, carcinoma of the lung with negative bronchi being, of course, a rarity. Coupling that with the peculiar histologic character we felt justified in continuing to call this a teratoma. There were extensive metastases to the liver and bone marrow, and the fifth lumbar vertebra was involved; there was nothing else of interest. The tumor was perfectly solid at the time of autopsy and nothing suggested at that time that it had ever been cystic. I am not quite clear from the surgical report whether it was cystic at the time of operation. The center was soft, but no fluid or air was reported.

Dr. Holmes: Were there any signs of x-ray treatment?

Dr. Mallory: The tumor was almost totally necrotic. We could hardly find a viable cell in the mediastinal tumor in contrast to the liver, where the histology was essentially that of the biopsy specimen.

Dr. Holmes: I suppose that the change in the fifth lumbar vertebra does represent a metastasis. However, it is wedge shaped, the reverse of what it should be with a pathologic fracture.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal

Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Richard M. Smith, M.D., *Chairman*
James P. O'Hare, M.D. William B. Breed, M.D.
Conrad Wesselhoeft, M.D. Oliver Cope, M.D.

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society

Editorial Board

Joseph Garland, M.D. Stephen Rushmore, M.D.
George R. Minot, M.D. Henry R. Viets, M.D.
Frank H. Lahey, M.D. Robert M. Green, M.D.
Shields Warren, M.D. Charles C. Lund, M.D.
George L. Tobey, Jr., M.D. John F. Fulton, M.D.
C. Guy Lane, M.D. A. Warren Stearns, M.D.
William A. Rogers, M.D. Dwight O'Hara, M.D.
Chester S. Keefer, M.D.

Associate Editors

Thomas H. Lanman, M.D. Donald Munro, M.D.
Henry Jackson, Jr., M.D.

Walter P. Bowers, M.D., Editor Emeritus
Robert N. Nye, M.D., Managing Editor
Clara D. Davies, Assistant Editor

Subscription Terms: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.04 per year, Boston funds; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Friday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

BACK TO THE LAND

When the conflict is over and the olive branch has blossomed and borne fruit, then, traditionally, the swords of the armies are beaten into ploughshares and their spears into pruning hooks. Or so said the Lord speaking through the tongues of Isaiah and of Micah. This, however, is only the second half of the allegory. It had first been necessary to beat certain ploughshares and pruning hooks into the swords and spears, and to place on priority lists the materials from which they had both been made.

It is implicit in the nature of democracy that when an aroused but unprepared and normally peace-loving people go to war they have to abandon their ploughs in the furrows (even before they are beaten into weapons). They never realize at the time that these implements are mighty weapons in their own right. Thus, at least, did Cincinnatus, and probably many a patriot, like the minuteman arrested in bronze beside the Concord River, in the midst of the ploughing season of 1775. Who planted the crops in those stirring days and later harvested them is left to the imagination, and our present predicament offers no satisfactory explanation. We may assume, however, that not all the machinery of agriculture was left to rust in the fields, — although that bucolic custom also has continued to the present day, — but that the women and boys and grown girls, being fit for the kingdom of God, did not look back, having put their hands to the plough. By some similar arrangement we must manage to get our own crops sown and harvested today.

With many of the commercial farmers failing us this year owing to the shortage of farm labor, it is necessary that a good deal of amateur gardening be undertaken, not all of it with benefit of press photography, and some of it resisting stubbornly the classification of "victory gardening." A considerable power of vernal enthusiasm is going to wilt under the summer sun, and since a great quantity of seed will be planted it is probable that more than the usual proportion will fall by the wayside or upon stony places or among thorns. Much of this crop will stand us in good stead, but it will be a wasteful crop, and better organization is going to be necessary if we are to keep potatoes in the barrel next winter.

The boys and girls of high-school age constitute the logical group to enlist for this particular, important effort, and so far as possible their task forces, adequately supervised, as their social activities should be adequately chaperoned, can be mobilized where they are most needed. This should include as little as possible in amateur victory gardening, praiseworthy as that effort is, and as much as possible in substantial farming, under the direction of capable farmers.

We are inclined to initiate anything with a burst of enthusiasm and often with a good many preliminary mistakes. A certain number of youngsters will be (and have been) put on farms where they will be more of a nuisance to the farmer than they will be a help. Some farmers view this back-to-the-farm movement with more concern than that with which they witnessed the on-to-the-city trek of earlier decades. Vacation help is limited, also, to only part of the farming season; it is available too late for planting and departs too early for the late harvest. It serves, nevertheless, two valuable purposes: it furnishes healthful summer vacations for the workers, and it makes a real and urgent contribution to the national effort.

The movement is under way; it has functioned quite satisfactorily already. Work camps have been successfully conducted, and many of the private summer camps are now adding farming to their activities. There is plenty of land on which to grow all the crops the world needs, but brains, organization and unceasing effort are required to keep it in production.

INVALID DIETS AND FOOD RATIONING

Ration Order 13, issued by the office of Price Administration under the date of February 9, 1943, is of interest to all who are concerned with diets for invalids. The order covers all canned, dried and frozen fruits and vegetables, and Article II, Section 2.5, reads as follows:

> Consumers who need more processed foods because of illness may apply for more points:
>
> (*a*) Any consumer whose health requires that he have more processed foods than he can get with War Ration Book No. 2, may apply for additional points. The application must be made on OPA Form R-315 by the consumer himself or by someone acting for him, and may be made in person or by mail. The application can be made only to the board for the place where the consumer lives. He must submit with his application a written statement of a licensed or registered physician or surgeon, showing why he must have more processed foods, the amounts and types he needs during the next two months, and why he cannot use unrationed foods instead.
>
> (*b*) If the board finds that his health depends on his getting more processed foods, and that he cannot use or cannot get unrationed foods, it shall issue to him one or more certificates for the number of points necessary to get the additional processed foods he needs during the next two months.

Form R-315 is likely to be confusing to patients, since it is titled "Sugar Special Purpose Application," having been developed to meet the demand for extra sugar for home canning. It is being used temporarily until a more adequate form is available.

This method of obtaining additional rationed foods will probably be modified in the future; if so, due notice of any change will be provided.

MEDICAL EPONYM

Tay-Sachs's Disease

Warren Tay (1843-1927) reported "Symmetrical Changes in the Region of the Yellow Spot in Each Eye of an Infant" (*Tr. Ophth. Soc. U. Kingdom*, 1:55–57, 1881). He writes:

> Mrs. L—— brought her infant, aet. 12 months, to the London Hospital, March 7th, 1881. When the baby was a fortnight or three weeks old, it was noticed to have very little power of holding its head up or of moving its limbs. Since that time the weakness had become more and more pronounced. . . . It seemed to me that its cerebral development was probably deficient, and I was induced to examine the eyes with the ophthalmoscope to ascertain whether there was any affection of the optic nerves. . . . I found the optic discs apparently quite healthy, but in the region of the yellow spot in each eye there was a conspicuous, tolerably defined, large white patch, more or less circular in outline, and showing at its centre a brownish-red, fairly circular spot, contrasting strongly with the white patch surrounding it.

Bernard Sachs (b. 1858) read a paper before the American Neurological Association in July, 1887, entitled "On Arrested Cerebral Development, with Special Reference to its Cortical Pathology" (*J. Nerv. & Ment. Dis.* 14:541–553, 1887). A portion of the article follows:

> The little girl S., who was but two years old at time of death, was the first-born of young and healthy parents. . . . Nothing abnormal was noticed until the age of two to three months, when the parents observed that the child was much more listless than children of that age are apt to be; that it took no notice of anything, and that its eyes rolled about curiously (there was evident nystagmus). Allowing for

some very slight vacillations, the child remained in practically the same condition up to the time of death. . . . The child as it grew older gave no signs of increasing mental vigor. It could not be made to play with any toy, did not recognize people's voices, and showed no preference for any person around it. During the first year of its life, the child was attracted by the light, and would move its eyes, following objects drawn across its field of vision; but later on absolute blindness set in.

Dr. Knapp, who made several ophthalmoscopic examinations of this case, reported the following unusual condition. . . ."Child two to three months; nystagmus vibratorius; pupils contracted as is usual with children at this age. Media clear, optic nerve discs pale. Fovea centralis, of a cherry red color, was surrounded by an intense grayish-white opacity. This opacity was most distinct in the vicinity of the fovea centralis, and for some little distance around it, but faded away gradually into normal retinal field." . . . "a further examination in May and June, 1886, revealed great changes. Child totally blind, optic nerves completely atrophied (discs as white as paper, with scarcely a trace of blood-vessels). Macula lutea essentially as before." . . .

During last summer (1886), the child grew steadily weaker, it ceased to take its food properly, its bronchial troubles increased, and finally, pneumonia setting in, it died August, 1886.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON INDUSTRIAL HEALTH

The Committee on Industrial Health will hold an all-day meeting at the Harvard Club of Boston on Saturday, April 24. Except for the omission of the dinner in the evening, this meeting will be similar to that held at the same place last November, with an entirely new program. Among the subjects covered will be the following: the methods used in establishing diagnoses of industrial poisoning; the late effects of craniocerebral trauma; the medical aspects of absenteeism in industry; the present status of the relation of heart disease to industry; epidemic keratoconjunctivitis; and the problems of women in industry. There will also be a panel discussion of the surgical, medical, insurance and preventive aspects of diabetes in industry. Other subjects will be added, and all papers will be delivered by recognized experts in their various fields. The program will start at 9:30 a.m. and should be concluded by 5:00 p.m.

Parking facilities will be available in the rear of the Club, on Newbury Street. There will be a registration fee of 50 cents to cover the cost of arrangements, and luncheon ($1.50 per plate) will be provided for those who make reservations. The facilities of the Harvard Club will be at the disposal of those in attendance, thus ensuring a comfortable and sociable atmosphere for all. Physicians, as well as personnel managers, nurses and others interested in safeguarding the health of workers in industry, are cordially invited to attend, and may register by addressing the Committee on Industrial Health, at 8 Fenway, Boston. Owing to wartime conditions, reservations for luncheons must be made at least forty-eight hours in advance.

All physicians who are interested in industrial health are assured a pleasant and profitable April 24. They should mark the date on their calendars, and send their checks for $2.00, covering registration and luncheon, to the committee before April 22.

DWIGHT O'HARA, *Chairman*

WAR ACTIVITIES

INDUSTRIAL MEDICINE

MEDICAL CARE FOR SMALL INDUSTRIES

In New York City a group of small industries has been considering a plan to provide medical care for their workers on a co-operative basis. The plan was drawn at their request by Group Health Co-operative, Incorporated, a nonprofit medical insurance organization.

The problem in small plants has been one of dealing with unfamiliar industrial hazards, inexperience with industrial medical service, and lack of funds to supply needed medical service. A solution seems to be some outside agency with the necessary organization to provide a common service for a number of small plants in a given area on a co-operative basis.

The plan drawn up would supply in-plant services through full-time industrial physicians (one physician for each 2000 employees) and nurses (one for each 500 employees). These in-plant services would include emergency treatment of accidents and illness while on the job, preemployment and periodic physical examinations, medical check-ups on employees returning to work after absence, supervision of plant hygiene, and co-operation in safety programs and health education. The industrial physician would render only emergency treatment in compensation cases, and the patient would, under the laws of New York State, be free to choose his own physician for subsequent care.

Closely correlated with these in-plant services is provision for home and office care and diagnostic specialist service for nonindustrial conditions, which constitute the major cause of absenteeism. The out-of-plant service would be rendered by a panel of doctors open to any licensed physician in the community. The employee would have completely free choice of any physician on the panel.

Because of objections raised by some employee groups to physical examinations conducted by industrial physicians, the plan provides alternately for pre-employment and periodic examinations to be rendered by the panel physician of the employee's choice.

It is hoped that close co-operation can be obtained between the in-plant and outside services through the medium of the central organization. The family doctor and the industrial physician should not operate as two sepa-

rate units, but as equal guardians of different phases of the employee's health.

It is intended that this service should be financed by the employer at a basic premium per employee of $1.42 each month. For each home visit by the physician of his choice, the employee would incur a charge of $1.00, payable directly to the physician.

In addition to this projected plan, Group Health Cooperative now has in operation a plan covering surgical, obstetrical and in-hospital medical care. This plan costs $9.60 a year for an individual or $24 for a family. The combination of these two plans would provide workers in war industries with comprehensive and integrated medical care at the plant, at home and in the hospital. — Reprinted from *Industrial Hygiene*, a bulletin issued monthly by the Division of Industrial Hygiene, United States Public Health Service.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR DECEMBER, 1942

Diseases	December 1942	December 1941	Five-Year Average*
Anterior poliomyelitis	2	7	3
Chicken pox	1444	1603	1512
Diphtheria	14	19	18
Dog bite	516	550	570
Dysentery, bacillary	6	16	16
German measles	190	68	14
Gonorrhea	286	273	359
Measles	1871	678	835
Meningitis, meningococcal	28	11	6
Meningitis, other forms	9	6	–†
Mumps	1080	1460	634
Paratyphoid infection	7	4	3
Pneumonia, lobar	327	208	367
Scarlet fever	1312	1171	731
Syphilis	489	335	420
Tuberculosis, pulmonary	249	241	274
Tuberculosis, other forms	14	26	29
Typhoid fever	3	9	8
Undulant fever	2	3	5
Whooping cough	1171	828	861

*Based on figures for preceding five years.
†Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

Anterior poliomyelitis was reported from: Palmer, 1; Springfield, 1; total, 2.

Anthrax was reported from: Middleboro, 1; total, 1.

Diphtheria was reported from: Boston, 1; Fall River, 2; Lexington, 1; Lowell, 2; Medford, 2; Methuen, 1; Newton, 1; Peabody, 1; Somerville, 1; Taunton, 1; Waltham, 1; total, 14.

Dysentery, bacillary, was reported from: Beverly, 1; Cambridge, 1; Peabody, 1; Waltham, 3; total, 6.

Meningitis, meningococcal, was reported from: Barnstable, 1; Boston, 4; Braintree, 1; Cambridge, 1; Camp Edwards, 1; Chelsea, 1; Fort Banks, 1; Fort Devens, 2; Gardner, 1; Lexington, 2; Lowell, 2; Lynn, 2; Mansfield, 1; Medford, 1; Middleboro, 2; Pittsfield, 1; Saugus, 1; Taunton, 2; Waltham, 1; total, 28.

Meningitis, other forms, was reported from: Boston, 1; Brookline, 1; Chicopee, 2; Cohasset, 1; Hardwick, 1; Leominster, 1; Quincy, 1; Springfield, 1; total, 9.

Paratyphoid infection was reported from: Boston, 2; Everett, 1; Lowell, 1; Melrose, 1; Spencer, 1; West Boylston, 1; total, 7.

Septic sore throat was reported from: Boston, 3; Cambridge, 1; Colrain, 1; Dedham, 1; Leominster, 1; Quincy, 1; West Springfield, 1; Worcester, 1; total, 10.

Tetanus was reported from: Norfolk, 1; total, 1.

Trachoma was reported from: Boston, 1; Cambridge, 1; total, 2.

Trichinosis was reported from: Boston, 2; Everett, 2; total, 4.

Typhoid fever was reported from: Boston, 1; Easton, 1; Medford, 1; total, 3.

Undulant fever was reported from: Cambridge, 1; Gloucester, 1; total, 2.

The general pattern of communicable-disease incidence for December shows no striking changes over that of last month.

Scarlet fever, whooping cough, measles and mumps are showing a decided upward trend. The scarlet-fever figure is a little less than the five-year average; measles, more than twice the average; and whooping cough well over the average and the highest figure since 1937, although still far from showing a record high.

Meningococcal meningitis has been increasing in incidence for the last two years; it is now four times the five-year average.

Other diseases that exceeded their five-year averages are German measles, mumps and syphilis.

Typhoid fever, paratyphoid infection, diphtheria and undulant fever, on the other hand, remain at low level. This month's diphtheria figure (14 cases) is next to the lowest December record since 1906.

Other diseases that fell below their five-year records are bacillary dysentery, lobar pneumonia, pulmonary tuberculosis, tuberculosis (other forms), gonorrhea, chicken pox and dog bite.

BOOK REVIEW

The Blood Bank and the Technique and Therapeutics of Transfusions. By Robert A. Kilduffe, A.M., M.D., and Michael DeBakey, M.D., M.S. 8°, cloth, 558 pp., with 214 illustrations and 1 color plate. St. Louis: The C. V. Mosby Company, 1942. $7.50.

Physicians in all branches of practice are using transfusions of blood, serum and plasma with increasing frequency. In war casualties the use of blood and its derivatives has been largely responsible for the salvage of the great numbers who would have died from shock thirty years ago.

The procedure of transfusion, simple as it is when properly done, is constantly fraught with dangers of a reaction. This work gives detailed consideration to the precautions that are necessary for the avoidance of such undesirable sequelae to transfusion.

With the advent of the blood bank, an entirely new factor has developed in the field of transfusion. It was to be hoped that stored blood would fill all the needs for fresh blood. But such is not the case, and in summarizing this aspect of the problem the authors say: "From the studies above discussed, it is apparent that although stored blood may be, and indeed has been shown conclusively to be, effectual in the treatment of shock and acute hemorrhage, it is definitely inferior to fresh blood in the transfusion treatment of acute and chronic infections, hemorrhagic states and the anemias. When stored blood is used in such conditions, the maximum storage period should preferably not exceed seventy-two hours."

Much of the text is devoted to the technics for transfusions, the operation of a blood bank and the preparation of blood derivatives, such as plasma and serum. These chapters have many illustrations to enable one easily to follow the methods described.

This is a timely book, and the authors have rendered great help to the people who must organize and run a transfusion service, whether in a large hospital or a fighting unit.

(Notices on page xi)

Is there any help for an overworked doctor?

YES—BIOLAC, because it saves you valuable time. It's a complete infant formula and there are no extra ingredients to calculate.

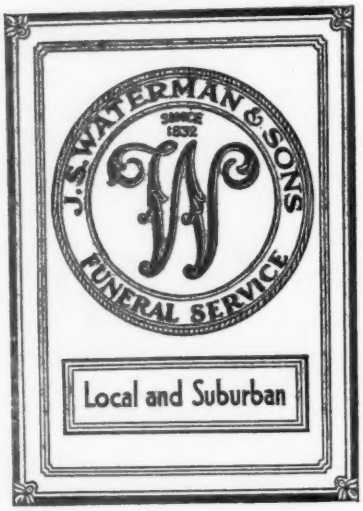
Biolac provides completely for all nutritional needs of the young infant except vitamin C.

Prescribe Biolac routinely to reduce the possibility of errors and contamination in formula preparation. It requires only simple dilution with boiled water . . . as you prescribe.

NO LACK IN BIOLAC

Borden's complete infant formula

• *Biolac is prepared from whole milk, skim milk, lactose, Vitamin B_1, concentrate of Vitamins A and D from cod liver oil, and ferric citrate. It is evaporated, homogenized, and* sterilized. *For professional information, write Borden's Prescription Products Division, 350 Madison Avenue, New York City.*



PROFESSIONAL PROTECTION

SINCE 1899 SPECIALIZED SERVICE

In addition to our Professional Liability Policy for private practice we issue a special MILITARY POLICY to the profession in the Armed Forces at a REDUCED PREMIUM

THE MEDICAL PROTECTIVE COMPANY
OF
FORT WAYNE, INDIANA
BOSTON OFFICE
11 Pemberton Sq., Room 303, Barristers Hall
Telephone CAPitol 0119
A. F. FOX, General Agent

The Original Enteric Coated

THESODATE (*Brewer*)

Theobromine Sodium Acetate†

CLINICALLY PROVED*
EFFECTIVELY ENTERIC COATED
DECIDEDLY LESS EXPENSIVE

PROVIDES 24-HOUR PROTECTION
Given 4 times daily, before meals and before retiring.

Thesodate tablets are available on prescription in 7½ grain tablets, with or without Phenobarbital (½ grain), or 3¾ grain tablets, with or without Phenobarbital (¼ grain), 100 in bottle.

*Literature on request.
†Thesodate capsules are available for those patients who may require extra medication.

BREWER AND COMPANY, INC. Worcester, Mass.

Pharmaceutical Chemists Since 1852

NOTICES

HOSPITAL COUNCIL OF BOSTON

The annual meeting of the Hospital Council of Boston will be held at the University Club, 40 Trinity Place, Boston, on Tuesday, April 13, at 12:30 p.m. There will be a discussion on food rationing by Edward Stiller and John G. Hamill, followed by a question period in which hospitals are urged to present questions.

The charge for luncheon will be $1.20. Reservations should be made before April 10 (LIB 8515).

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, April 20, at 12 m. Dr. Robert Fleming, instructor in psychiatry, Harvard Medical School, will speak on the subject, "The Medical Aspects of Alcoholism."

Physicians are cordially invited to attend.

CHILDREN'S HOSPITAL

On Friday, April 9, at 5 o'clock, in the amphitheater of the Children's Hospital, Dr. Harry M. Zimmerman, associate professor of pathology, Yale University Medical School, will speak on the subject, "Histopathology of Convulsive Disorders in Children."

This meeting is open to the medical public.

NEW ENGLAND SOCIETY OF ANESTHESIOLOGY

The next meeting of the New England Society of Anesthesiology will be held in the amphitheater of the White Surgical Building, Massachusetts General Hospital, on Tuesday, April 13, at 8 p.m. Dr. Sidney C. Wiggin will speak on the subject, "Spinal Anesthesia for Children."

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, APRIL 4

MONDAY, APRIL 5

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, APRIL 6

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

8:15 p.m. High-Protein Diet: Clinical considerations. Dr. George W. Thorn. Greater Boston Medical Society. Beth Israel Hospital auditorium.

WEDNESDAY, APRIL 7

*9:00–10:00 a.m. Diabetic clinic. Dr. Joseph Rosenthal. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Clinicopathological conference. Children's Hospital.

THURSDAY, APRIL 8

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

7:00 p.m. New England Hospital for Women and Children. Monthly clinical conference and meeting of staff.

FRIDAY, APRIL 9

*9:00–10:00 a.m. Traumatic Shock. Dr. J. C. Aub. Joseph H. Pratt Diagnostic Hospital.

*5:00 p.m. Histopathology of Convulsive Disorders in Children. Dr. Harry M. Zimmerman. Children's Hospital, Boston.

(Notices continued on page xiii)

WAR WORKERS

put back on jobs quickly when you prescribe a

SPENCER SUPPORT

as aid to treatment of

HERNIA

FATIGUE
Due to Overwork

ENTEROPTOSIS
With Symptoms

LOW VITALITY

BACK INJURY

POSTOPERATIVE
Convalescence

WRONG POSTURE
and Symptoms

Spencer Sacroiliac Support designed for this woman.

Spencer Sacroiliac Support designed for this man.

Since each Spencer Support is individually designed of non-stretchable material to meet the specific needs of the patient, it can be—and IS—*guaranteed* never to lose its shape. Why prescribe a support that soon stretches out of shape and becomes useless?

Spencers are light, comfortable, easily laundered. Every Spencer is designed to improve posture and provide the required degree of abdominal and back support.

Spencer Supports are never sold in stores. For a Spencer Specialist, look in telephone book under "Spencer Corsetiere" or write direct to us.

SPENCER *INDIVIDUALLY DESIGNED*

Abdominal, Back and Breast Supports

SPENCER INCORPORATED,
137 Derby Ave., New Haven, Conn.
In Canada: Rock Island, Quebec.
In England: Spencer (Banbury) Ltd., Banbury, Oxon.

May We Send You Booklet?

Please send me booklet, "How Spencer Supports Aid the Doctor's Treatment."

.....M. D.

Address A-4

63rd Year

RING SANATORIUM AND HOSPITAL

ARLINGTON HEIGHTS, MASS.

For the diagnosis, care and treatment of mental, nervous and chronic medical diseases.

Facilities for all accepted therapeutic measures, including artificial fever and shock therapy.

Outpatient department for referred cases only. Moderate, all-inclusive rates.

VOLTA R. HALL, M.D., MARTHA BRUNNER, M.D.
Resident Physicians

HALLAM T. RING, *Administrator*

163 Hillside Avenue Tel. ARL 0081

Dr. Taylor's Private Hospital

For the Treatment of
ACUTE or CHRONIC
ALCOHOLISM

House well equipped and furnished, skilled attendants, good food and comfortable rooms at moderate rates.

Methods of treatment are those proved best after 30 years' successful experience.

FREDERICK L. TAYLOR, M.D.
45 Centre Street, Boston, Mass.
Near Dudley Street Terminal Roxbury District

WOODSIDE COTTAGES
Framingham, Mass.

A sanitarium specially adapted for nervous and convalescent patients who need rest and upbuilding in normal surroundings.
No committed mental cases.
ARTHUR H. WARD, M.D., *Medical Director*

Glenside

JAMAICA PLAIN, BOSTON, MASS.
A small, attractively located sanitarium for nervous, mild mental or chronic illnesses.
MABEL D. ORDWAY, M.D.
6 Parley Vale Tel. ARN 0044

Wiswall Sanatorium

203 Grove Street
Wellesley, Mass.

A small group of attractive buildings for the care and treatment of nervous and mild mental diseases.

Facilities for training and diversion under the direction of a competent therapist.

E. H. WISWALL, M.D.
Superintendent
HALE POWERS, M.D.
Resident Physician
Tel. WEL 0261

WESTWOOD LODGE
Westwood, Mass.

A modern private sanitarium within fifteen miles of Boston, for the treatment of nervous and mild mental diseases; also for those in need of rest under medical supervision. Separate buildings make possible a satisfactory grouping of patients. The buildings, which include one devoted exclusively to occupational therapy, are surrounded by over one hundred acres comprising woodlands, gardens and pine groves.

Superintendent
WILLIAM J. HAMMOND, M.D.

Resident Physicians
SIDNEY M. BUNKER, M.D.
ELSIE S. NEUSTADT, M.D.

Perkins School

LANCASTER, MASS.

Devoted to the scientific understanding and education of children of retarded development.

Five homelike and attractive buildings surrounded by 85 acres of campus and gardens.

Medical Direction *Experienced Staff*
FRANKLIN H. PERKINS, M.D.

ADAMS HOUSE
(OF ADAMS NERVINE)
Established 1877
A sanitarium-clinic for the psychoneuroses exclusively
Located in beautiful suburban Boston
JAMES MARTIN WOODALL, M.D.
Medical Director
990 Centre Street
Boston (Jamaica Plain), Mass.

Baldpate, Inc.

Georgetown, Mass.

GEO 2131 — Boston Office KEN 8100

For the treatment of psychoneuroses, personality disorders, psychoses, alcoholism and addictions.

Psychotherapy is the basis of treatment; other methods such as *shock therapy, malaria* and *fever box* are used when indicated.

Occupation under a trained therapist, diversions and outdoor activities.

H. C. SOLOMON, M.D., *Psychiatrist*
G. M. SCHLOMER, M.D., *Medical Director*
H. JANE MONTZINGO, M.D.
EUGENE L. SWAN, M.D.
Resident Physicians

A Request for Change of Address

Must reach us at least a week before the date of issue with which it is to take effect. Duplicate copies cannot be sent to replace those undelivered through failure to send such advance notice. With your new address be sure to send us the old one, enclosing, if possible, your address label from a recent copy.

NEW ENGLAND JOURNAL OF MEDICINE
8 Fenway, Boston, Mass.

CHARLES B. TOWNS HOSPITAL

Serving the Medical Profession for Over 40 Years

FOR ALCOHOLISM AND DRUG ADDICTION EXCLUSIVELY

Definite Treatment -- Fixed Charges -- Minimum Hospitalization

293 CENTRAL PARK WEST, NEW YORK, N. Y. -- Tel: SChuyler 4-0770

(*Hospital Literature*)

SATURDAY, APRIL 10

•10:00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

•Open to the medical profession.

APRIL 13. New England Society of Anesthesiology. Page xi.

APRIL 13. Hospital Council of Boston. Page xi.

APRIL 20. South End Medical Club. Page xi.

MAY 19–25. American Board of Obstetrics and Gynecology. Page xii, issue of March 4.

MAY 24–27. War Conference. Page ix, issue of March 25.

MAY 25 and 26. Massachusetts Medical Society. Hotel Statler, Boston.

JUNE 4 and 5. American Board of Ophthalmology. Page xii, issue of March 4.

DISTRICT SOCIETIES

BRISTOL SOUTH

MAY 6. New Bedford.

ESSEX NORTH

MAY 5.

ESSEX SOUTH

APRIL 7. Addison Gilbert Hospital, Gloucester.

MAY 5. Salem Country Club.

FRANKLIN

MAY 11. Annual meeting.

Meetings are held at 11:00 a.m. at the Franklin County Hospital, Greenfield.

HAMPSHIRE

MAY 5.

MIDDLESEX EAST

MAY 5. Bear Hill Golf Club, Stoneham, 6:30 p.m.

MIDDLESEX NORTH

APRIL 28.

JULY 28.

PLYMOUTH

APRIL 15. Bridgewater State Farm.

MAY 20. Lakeville.

WORCESTER

APRIL 4. Hahnemann Hospital, Worcester.

MAY 12. Annual meeting.

WORCESTER NORTH

APRIL 28.

JULY 28.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Poems of John Chalmers Da Costa. Edited by Frederick E. Keller, M.D. 12°, cloth, 85 pp. Philadelphia: Dorrance and Company, 1942. $1.50.

John Chalmers Da Costa was an eminent surgeon and teacher in Philadelphia. It was recently discovered that he was a poet as well, and here are collected for the first time in book form a selection of his poems.

Blood Substitutes and Blood Transfusion. Edited by Stuart Mudd, M.D., professor of bacteriology, University of Pennsylvania School of Medicine, Philadelphia; and William Thalhimer, M.D., director, Human Serum Division, Public Health Research Institute of the City of New York, Incorporated. 8°, cloth, 407 pp., with 97 illustrations, 6 charts, 60 tables and 6 graphs. Springfield, Illinois: Charles C Thomas, 1942. $5.00.

This symposium by seventy American investigators furnishes up-to-date knowledge on the vital questions of transfusion and the use of blood plasma in both civilian and military life.

Channing Sanitarium

ESTABLISHED 1879

A pleasant country community of cottages built for the homelike care and treatment of nervous patients. Separate cottage for the care of convalescent nonmental patients. Occupational therapy. Tennis court. Sports building.

JACKSON M. THOMAS, M.D., *Superintendent* — CLIFFORD G. ROUNSEFELL, M.D., *Resident Physician*

WELLESLEY, MASSACHUSETTS

Telephone — Wellesley 0464

BREAST MILK

may be obtained at the offices and laboratory of

The

Directory for Mothers' Milk

Incorporated

221 Longwood Avenue, Boston

Telephone BEA 5330

Prices will be adjusted to make the milk available to all who need it

Sent packed in ice to all parts of New England

Bournewood Hospital

300 SOUTH STREET, BROOKLINE, MASS.

Established 1884

For a limited number of cases of mental and nervous diseases

POST OFFICE, CHESTNUT HILL

Telephone PAR 0300

GEORGE H. TORNEY, M.D.

Washingtonian Hospital

41 WALTHAM STREET, BOSTON, MASS.

Founded 1841

A nonprofit-making, endowed institution, reorganized, for the

MODERN TREATMENT OF MEN SUFFERING FROM ACUTE OR CHRONIC

ALCOHOLISM

JOSEPH THIMANN, M.D., *Medical Superintendent*

MERRILL MOORE, M.D., *Director of Research*

Visits by Psychiatric and Neurological Staff

Consultants in Medicine, Surgery and the Specialties

Rates Moderate

For information: consult the Medical Superintendent

Telephones: HAN 1750 and 1751

During Food Shortages...

It is well to bear in mind that dried brewers yeast, weight for weight, is the richest food source of the Vitamin B Complex. For example, as little as 1 level teaspoonful (2.5 Gm.) Mead's Brewers Yeast Powder supplies:

45% of the average adult daily thiamine allowance
8% " " " " " riboflavin allowance
10% " " " " " niacin allowance

— in addition to the other factors that occur naturally in yeast such as pyridoxine, pantothenic acid, etc. Following are suggestions for palatably mixing 1 level teaspoonful Mead's Brewers Yeast Powder:

(1) Shake in cocktail shaker with 4 ounces of milk (with or without 1 level teaspoonful sugar and cocoa).

(2) Stir with fork into ¾ ounce of ketchup or chili sauce. Optional, add a few drops of lemon juice.

(3) Stir with fork into 3 ounces of soup (preferably thick soups such as bean, pea, oxtail, beef, etc.).

(4) Spread on bread with 2 to 3 times the amount of peanut butter.

(5) Add 1 level tablespoonful (and a little extra salt) to 2 cups of meat stock gravy.

Mead's Brewers Yeast is supplied in 6-oz. bottles, economically. At the rate of even 2 level teaspoonfuls per day, per adult, a bottle should last over a month. Also supplied in 6-grain tablets. 250 and 1000 tablets per bottle. All Mead Products are advertised only to the medical profession.

Why not try this recipe at home? It makes good gravy taste meatier.
Send for tested wartime recipes containing yeast.

MEAD JOHNSON & COMPANY, Evansville, Ind., U.S.A.